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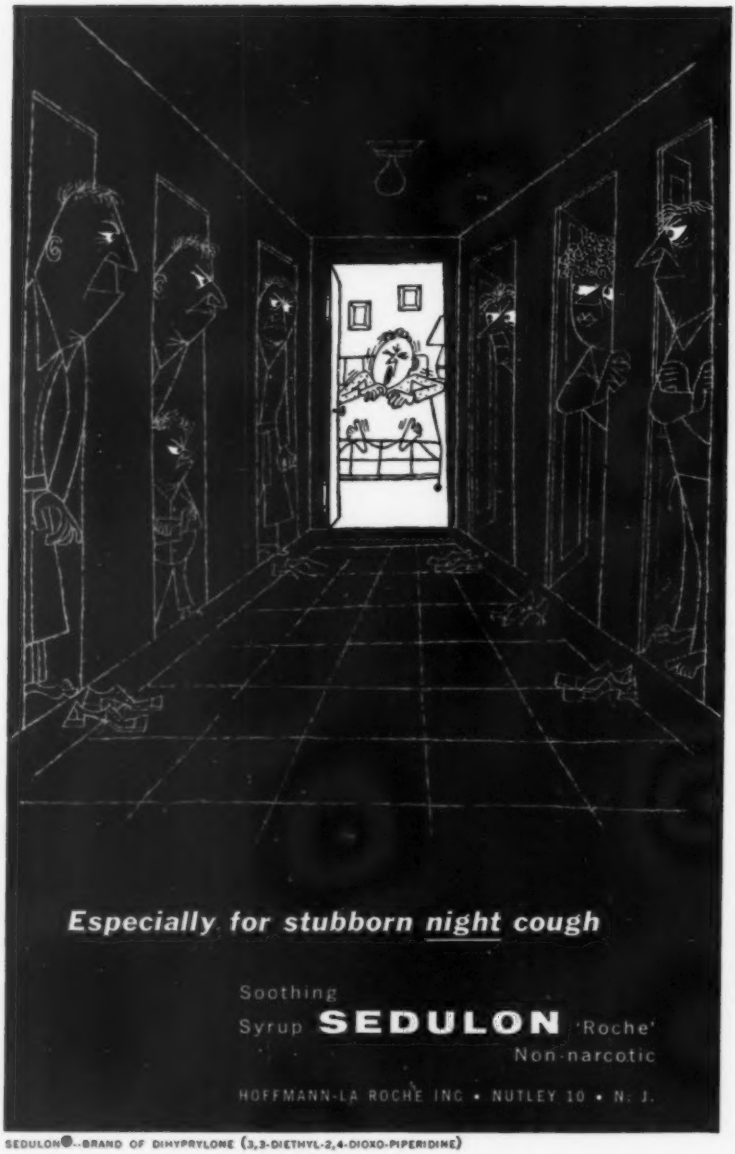

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The Journal of Pediatrics

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THE INFREQUENT INCIDENCE OF NONPARALYTIC POLIOMYELITIS

E. B. SHAW, M.D., AND MARCIA LEVIN, M.D.*

SAN FRANCISCO, CALIF.

IT HAS long been our conviction that whenever the diagnosis of poliomyelitis can be established on clinical grounds that muscular weakness can be objectively demonstrated in nearly every case at one time or another to a greater or lesser degree.[1]

In this present study we have examined the course of 798 patients admitted to the Communicable Disease Service of Children's Hospital, San Francisco, from July 1, 1950, to July 1, 1953. These are consecutive cases under the care of a number of different physicians, but the great majority of them have been the responsibility of one of us. We had daily knowledge of each case during the acute phase of the disease and none has been excluded in which the clinical and laboratory evidence persuasively supported the diagnosis. Those patients admitted for care after the acute febrile stage have not been included because the admission diagnosis was unmistakable and they would serve simply to augment the size of the series without contributing to the point at issue.

Table I summarizes our experience during the period July 1, 1950, to June 30, 1952.

From the Communicable Disease Department, Children's Hospital, San Francisco, and the Department of Pediatrics, University of California Medical School.

*Research Fellow in Communicable Diseases, Children's Hospital, San Francisco.

Table II covers the epidemic period July 1, 1952, to Dec. 31, 1952.

Table III includes the interepidemic period Jan. 1, 1953, to June 30, 1953, in which the problem of diagnosis in the winter and spring was somewhat more difficult but in which we encountered some cases of unusual severity.

We do not propose to discuss this case material in detail but in these tables have presented sufficient data to permit comparison with reports of other observers.

In 501 cases included in Table I, 484 (96.6 per cent) were paralytic and only seventeen (3.4 per cent) were nonparalytic. In this series 164 were admitted in the preparalytic phase and in this number were obviously to be found all of the nonparalytic sequelae (the others having been admitted after paralysis was apparent). Thus 10.4 per cent of preparalytic admissions escaped detectable weakness.

Throughout we have segregated local and nonlocal patients, the former being admitted from San Francisco and environs and the latter from more remote sources in Northern California. It was thought that local patients might be referred on minimal evidences of disease and thus contribute a higher proportion of nonparalytic

In Table II—the summer epidemic of 1952—in a total of 251 patients, 240 (95.6 per cent) were paralytic and 11 (4.4 per cent) were nonparalytic. Of these, 104 were admitted preparalytic of which the 11 nonparalytic cases constituted 10.6 per cent. Sixty-eight of local origin were nonparalytic compared to five (7 per cent) of the nonlocal. outcome. This seems to have been true although the numerical difference is not great. Twelve (13.8 per cent) of the preparalytic admissions

TABLE I. ADMISSIONS, JULY 1, 1950, TO JUNE 30, 1952

ADMISSION STATUS	ORIGIN	NUMBER OF CASES	OUTCOME		NUMBER IN RESPIRATOR	FATAL
			PARALYTIC	NONPARALYTIC		
Preparalytic	Local	87	75	12 (13.8%)	2	1
	Nonlocal	77	72	5 (7%)	2	1
Paralytic	Local	58	58		15	10
Bulbar and bulbospinal	Nonlocal	52	52		18	13
Spinal	Local	99	99		15	7
	Nonlocal	128	128		14	2
Totals	All cases	501	484 (96.6%)	17 (3.4%)	66 (13.1%)	34 (6%)

TABLE II. ADMISSIONS, JULY 1, 1952, TO DEC. 31, 1952

ADMISSION STATUS	ORIGIN	NO. OF CASES	OUTCOME		NUMBER IN RESPIRATOR	FATAL	SPINAL FLUID CELLS	
			PARALYTIC	NONPARALYTIC			INCREASED	NORMAL
Preparalytic	Local	68	60	8 (11.8%)	4	0	56	2
	Nonlocal	36	33	3 (8.4%)	0	0	25	0
Paralytic	Local	39	39	0	6	4	22	2
Bulbar and bulbospinal	Nonlocal	21	21	0	2	0	10	2
Spinal	Local	53	53	0	7	2	39	0
	Nonlocal	34	34	0	9	0	17	2
Totals		251	240 (95.6%)	11 (4.4%)	28 (11.2%)	6 (2.4%)	169 (95%)	8 (5%)

TABLE III. ADMISSIONS, JAN. 1, 1953, TO JUNE 30, 1953

ADMISSION STATUS	ORIGIN	NO. OF CASES	OUTCOME		NUMBER IN RESPIRATOR	FATAL	SPINAL FLUID CELLS	
			PARALYTIC	NONPARALYTIC			INCREASED	NORMAL
Preparalytic	Local	12	9	3 (25%)	2	0	12	0
	Nonlocal	1	1	0	0	0	1	0
Paralytic	Local	8	8	0	3	3	3	0
Bulbar and bulbospinal	Nonlocal	2	2	0	1	0	0	0
Spinal	Local	11	11	0	1	0	6	0
	Nonlocal	12	12	0	3	0	10	0
Totals		46	43 (93.5%)	3 (6.5%)	10 (21.7%)	3 (6.5%)	32 (100%)	0

preparalytic admissions were of local origin, 60 were paralytic (88.2 per cent) and 8 were nonparalytic (11.8 per cent). Of 36 nonlocal preparalytic cases, 33 (91.6 per cent) were paralytic and 3 (8.4 per cent) were nonparalytic.

In Table III—interepidemic winter and spring, 1953—there were 46 patients of which 43 (93.5 per cent) were paralytic and 3 (6.5 per cent) were nonparalytic. Twelve of these were local and admitted preparalytic of which 9 (75 per cent) were paralytic and 3 (25 per cent) were nonparalytic. The single nonlocal preparalytic case developed definite weakness.

TABLE IV. SUMMARY

Total preparalytic admissions, July 1, 1950, to June 30, 1953	281	
Of these, nonparalytic course	31	(11%)
Total cases July 1, 1950, to June 30, 1953	798	
Of these, nonparalytic course	31	(3.9%)

Table IV summarizes the three preceding tables. In a total of 798 consecutive admissions, 31 (3.9 per cent) were nonparalytic which were to be found among 281 preparalytic admissions (11 per cent).

These results reinforce our conviction that only a small proportion of those patients in whom the original diagnosis can be established will completely escape muscle weakness. This is considerably at variance with opinions commonly expressed.

The following data from the California State Health Department indicate the reported incidence of poliomyelitis and of over-all accompanying paralysis in this state.

Date	*No. Cases*	*No. Nonparalytic*
4/1/48-3/31/49	6,044	1,652 (28%)
4/1/49-3/31/50	2,624	878 (33.5%)
4/1/50-3/31/51	2,312	684 (29.5%)
4/1/51-3/31/52	3,203	961 (30%)
4/1/52-3/31/53	4,284	1,576 (36.8%)
5-Year Total	18,467	5,751 (31.2)%
4/1/53-8/ 8/53	881	460 (52.3%)

As a matter of fact we believe that even our small number of nonparalytic cases considerably overstates the actual proportion of these because almost without exception they were found among those in which the initial symptomatology was mild and equivocal. We have included every case in which the clinical diagnosis seemed tenable but in some of these, known exposure, especially sibling exposure, helped to establish a diagnosis which might otherwise have been missed entirely. Occasionally the diagnosis was supported only by mild symptomatology and failure to establish an alternative diagnosis. Similarly, failure to detect muscle weakness sometimes depended upon a too short period of observation without opportunity for follow-up. Inescapably the inclusion of all manner of mild illnesses reported as poliomyelitis might increase the number of nonparalytic cases to almost any imaginable figure.

In Table V we have recorded at least a partial list of those patients referred to the hospital with a valid suspicion of poliomyelitis. Sometimes, as commonly occurs in every center for the care of this disease, the reasons for suspecting the diagnosis were so unconvincing as to make an alternative diagnosis apparent at the time of admission. A diversity of conditions appear in this list of suspect cases; in the majority an alternative diagnosis could quickly be established. Our greatest concern was that among these might be some who were nonparalytic poliomyelitis and we were content to accept as polio a

few simply because of our failure to establish another diagnosis. We believe that all those included in Table V are most unlikely to be poliomyelitis.

Epidemic poliomyelitis is coincident with arthropod-borne encephalomyelitis—of which we had a number of cases. In the group of suspects there were ten cases of encephalitis in which the exact etiology could not be determined but in these the central nervous system infection bore little resemblance to the clinical picture of poliomyelitis.

TABLE V. DIFFERENTIAL DIAGNOSES (Admitted With Suspect Diagnosis of Poliomyelitis in Which an Alternative Diagnosis Could Be Established)

(1) Respiratory and gastrointestinal infections (usually with meningism)	82
(2) Miscellaneous disease of bones and joints (20), rupture I.V. disk (1), rheumatic fever (2), cervical myositis (2), cellulitis (1), abscess of thigh (1), scurvy (1)	28
(3) Systemic disease: fever unknown origin (4), exanthem subitum (3), leptospirosis (2), infectious mononucleosis (1), nephritis (1), hepatitis (2), disseminated lupus (1), dermatomyositis (1)	15
(4) Central nervous system disease: hysteria and anxiety state (5), cerebral or subdural hemorrhage (4), neoplasm of brain or cord (6) peripheral neuritis (1), Guillain-Barré syndrome (6), mumps meningitis (19), bacterial meningitis (12), Meningitis—exact etiology? (4), Western equine and St. Louis encephalomyelitis (19), encephalitis, undetermined etiology (10)	86
Total	211

The analysis of any series of cases with respect to outcome must necessarily involve a precise definition of terms. One must first define the criteria which establish the diagnosis and, second, must define what constitutes paralysis.

The diagnosis of poliomyelitis is a matter of clinical opinion. There is no doubt that innumerable mild infections, below the threshold of clinical recognition, are due to the specific virus and that these subclinical and inapparent infections account for the presence of antibodies in the general population. Faber and Amoss[2] state that probably 1,000 such occur for every one which is recognizable. *Infection* which is inapparent must be distinguished from *disease* which is accompanied by recognizable symptoms and signs.

Clinical poliomyelitis consists of a short febrile, influenza-like course of about five days without pathognomonic symptoms: mild malaise, fever which is usually not high, headache, minor gastrointestinal symptoms, muscle pains and soreness, etc. Examination reveals slight neck stiffness which is usually quite definite but falls short of the marked rigidity of meningitis. Tremulousness is a common finding. Changes in reflexes and other localizing neurological findings are of little importance until about the time of appearance of muscle weakness. Laboratory findings are not revealing—except for their negative value—apart from the spinal fluid cell count which will show some elevation in the majority of cases. In Tables II and III normal spinal fluids were found in less than 5 per cent which is in accord with the usual picture. Normal spinal fluid findings will not indisputably exclude the diagnosis.

As the fever subsides, whether or not actual weakness can be detected, there is almost invariably an increase in neck and back stiffness together with soreness and stiffness ("spasm") of the musculature of the extremities. This *late oncoming stiffness* is perhaps

the most characteristic symptom which distinguishes poliomyelitis from other central nervous system diseases such as mumps meningo-encephalitis and other benign forms of meningitis, arthropod-b o r n e encephalomyelitis, treated bacterial meningitis, and other conditions with which this disease might be confused.

The summation of the positive clinical evidences, especially during epidemics, will usually lead the experienced observer to a perfectly sound and tenable diagnosis of poliomyelitis. Unfortunately this is not susceptible to routine serological confirmation.

The detection of weakness is also a matter of clinical judgment. In the early stage of infection it is inadvisable to attempt to determine exactly the extent of muscle weakness because the patient must be protected from exertion and fatigue. Careful observation may reveal weakness but detailed evaluation is of no particular moment at this time.

As the acute symptoms subside and muscle spasm begins to abate, the trained physical therapist can readily evaluate muscle strength. The clinician can easily and rapidly test muscle power by rather simple measures which will fairly accurately reproduce the results of the more time-consuming routine of the physical therapist.

The following can be carried out in a few minutes: The patient lies recumbent on an examining table. While his feet are held down against the table he is instructed to fold his arms across his chest and to rise to a sitting position. He is carefully observed for weakness or imbalance of the anterior neck muscles, for weakness and imbalance of the abdominal muscles, and for shift of the umbilicus which reveals abdominal weakness.

The patient now sits erect with his legs over the side of the table while the examiner stands in front of him with the patient's head against the examiner's chest and they grasp hands. Against moderate resistance the patient now attempts all movements of the upper extremities, carrying on these movements smoothly and symmetrically while the observer notes the relative strength and such things as "winging" of the scapulas and distortion and imbalance as he looks down the spine.

The patient is now assisted to stand first on one foot and then on the other, to rise on either tiptoe and on either heel, and then, with support, to execute a full squat with either lower extremity.

After convalescence is sufficiently established, the patient is observed while walking for revealing weakness of extremity and trunk muscles.

Significant weakness should be completely objective and readily confirmed by one examiner. Many patients who are eager for activity, who can readily walk out of the hospital, and who are persuasively nonparalytic will thus be found to have very definite muscle weakness which cannot be detected while they are recumbent in bed. The detection of mild weakness very early in the disease is not a matter of great importance and there is at least the hope—usually ill founded—that this will disappear during the acute course. It is of considerable importance, however, to be absolutely certain regarding muscle power by the time the patient is discharged and throughout

a period of later study—which we continue for three years at increasing intervals, even in those mildly affected. Severe degrees of muscle weakness are readily detected and may be appropriately dealt with by conventional rehabilitation measures. Mild degrees of weakness may be easily overlooked, characterize the vast majority of "nonparalytic" sequelae, and may lead to late disability and deformity which are completely preventable.

There are many examples of late impairment which fall within this preventable group. The muscle which shows slight weakness but is opposed by muscles which have some residual tightness and diminished range may function fairly normally early in convalescence. With fatiguing activity and especially during periods of rapid growth, the imbalance may be exaggerated so that significant and sometimes severe sequelae only then become apparent.

The patient who has only slight imbalance of spinal, abdominal, and neck muscles may eventually develop dismal spinal scoliosis. Minimal weakness of gastrocnemius or anterior tibial muscles with accompanying muscle spasm, muscle shortening, and the overuse of opposing muscles or of substituted muscle action may lead to serious disability. With the continuance of growth and activity severe deformities of the foot may result from muscle weakness and spasm which is initially not great.

There are innumerable examples in which these combinations of mild weakness and loss of normal muscle range due to spasm and secondary fibrosis will provoke imbalance and progressive disability and deformity. These can only be anticipated and prevented by early, careful, and repeated examinations.

The comparatively few cases in which definite weakness could not be demonstrated at any time were almost invariably those in which the initial diagnosis depended upon symptoms and signs which were mild, vague, or inconclusive. We have attempted to make an unprejudiced analysis which would include every patient for whom the diagnosis was accepted, even those with dubious findings in whom we simply failed to establish an alternative diagnosis. Accordingly, the proportion of nonparalytic cases is somewhat larger than if the etiology were a matter of fact instead of a matter of opinion. These borderline cases occupy the zone between those which are clinically detectable and the great number of inapparent infections.

COMMENT

We should certainly not wish to belabor the thesis that clinically recognizable poliomyelitis is invariably followed by detectable muscle weakness—although it is our belief that by and large this is true. The matter of greatest importance is that nonparalytic outcome should not be expected to occur in many patients for, if muscle weakness is regarded as *probable*, careful examination may reveal paralytic symptoms in which adequate therapy will greatly improve the end result. That different clinicians who may employ different criteria may have somewhat different results percentagewise does not alter the importance of this conclusion. It should be noted that we have called paralytic all of those in which any weakness

could be discovered at any time without regard to the final outcome. In the vast majority, however, weakness, once apparent, has been objectively demonstrable for at least two or three months.

SUMMARY

There has been reported a series of 798 consecutive cases of poliomyelitis seen during a three-year period. Some data have been incidentally included to indicate mortality, the use of the respirator, and the spinal fluid cell count for comparison with other reported series.

These patients have been analyzed for the incidence of nonparalytic recovery. Only thirty-one (3.9 per cent) of these patients ran a nonparalytic course as compared with the statewide nonparalytic rate for the five-year period of 31.2 per cent. Two hundred eighty-one patients were admitted preparalytic, and, of these, the thirty-one nonparalytic patients constituted 11 per cent.

Mild degrees of paralysis may be found only by careful examination and follow-up study.

Some weakness of musculature should be expected, even though this may not be invariable in most patients in whom the clinical diagnosis can be established.

The detection and adequate treatment of minor paralysis may readily prevent significant late sequelae.

REFERENCES

1. Shaw, Edward B., and Thelander, H. E.: Clinical Concept of Poliomyelitis, Pediatrics **4**: 277, 1949.
2. Faber, H. K., and Amoss, W. L.: Acute Poliomyelitis, in Tice's Practice of Medicine, Hagerstown, Md., 1953, W. F. Prior Co., Inc. vol. V, p. 343.

ADDENDUM

After the completion of this manuscript, a paper appeared in the *Journal of the American Medical Association* (**152**: 1505, 1953) by Moskowitz and Kaplan. The authors comment on the frequency with which patients dismissed from Grasslands Hospital as nonparalytic showed various sequelae during routine follow-up examinations. Seventy-five patients with nonparalytic poliomyelitis were examined one and one-half to six years after the onset of the illness of which 38.6 per cent were found to have minimal weakness in one or more muscle groups.

This retrospective study suggests some conformity with our opinion that an even higher percentage might show significant muscle weakness earlier in convalescence.

HYPOPLASTIC ANEMIA FOLLOWING EXCHANGE TRANSFUSION FOR ERYTHROBLASTOSIS FETALIS ASSOCIATED WITH ISOIMMUNIZATION TO BLOOD GROUP FACTOR "A"

Treatment With Cortisone

E. Albert Moody, M.D.
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ALTHOUGH the occurrence of erythroblastosis fetalis resulting from isoimmunization of the mother with Group "O" blood by fetal "A" agglutinogens has been established beyond doubt,[1, 2, 3, 4] cases of this nature continue to surprise and puzzle the physician. The physician is now sufficiently aware of the occurrence of isoimmunization of the Rh-negative mother by an Rh-positive fetus to check anti-Rh (positive) antibodies during pregnancy. When positive titers are demonstrated, the infant is observed closely after birth and proper treatment instituted should the signs of hemolytic disease appear. When, however, the occasional isoimmunization with major blood groups occurs, the physicians are usually completely surprised and may arrive at the proper diagnosis with considerable delay and confusion. The direct Coombs test is no longer a reliable guide in these cases as it is often negative.[5] The following case illustrates some of the difficulties encountered in these cases.

CASE REPORT

T. B. was born on Dec. 29, 1952, of a 24-year-old para ii, gravida iv, white mother. The mother's previous pregnancies had been uneventful except that her first baby had died at one day of age of unknown cause. The mother was known to be type O Rh negative. Titers taken on June 24, Nov. 13, and Dec. 8, 1952, failed to reveal any anti-Rh-positive antibodies in the mother's sera. Delivery was by cesarean section because of previous operative deliveries. At birth, the baby cried spontaneously and did not appear abnormal, but within an hour became pale and listless. At this time, the red blood cell count was 3.5 million, hemoglobin was 10.8 grams, white blood cell count was 22,100 with 61 per cent neutrophils, 35 per cent lymphocytes, 4 per cent monocytes. There were 3 per cent nucleated red blood cells. The blood type was Group "A" Rh positive. The direct Coombs developing test was negative. A post-partum maternal serum sample failed to disclose any anti-Rh-positive antibodies.

The baby was given 50 c.c. of Group "A" Rh-negative blood through an ankle vein by a physician. On December 30, the skin had become icteric and the liver was palpable 1 cm. below the left costal margin. The remainder of the examination was normal. The hemoglobin was 12.2 grams and the serum bilirubin 16.6 mg. per cent. On December 31, the hemoglobin had fallen to 9.4 grams and the serum bilirubin had risen to 24 mg. per cent. An exchange transfusion was performed using Group "A" Rh-negative blood. Due to technical difficulties, only 330 c.c. of blood was withdrawn and 390 c.c. replaced. On Jan. 1, 1953, the hemoglobin had fallen again to 7.5 grams and the serum bilirubin was 18.5 mg. per cent. A repeat exchange transfusion was per-

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formed through the right femoral vein. This transfusion was more successful and 650 c.c. of blood was removed and 720 c.c. of Group "A" Rh-negative blood replaced. On January 2, the hemoglobin was 6.1 grams, and he was given two simple transfusions of Group "A" Rh-negative blood through a scalp vein. Three days later the hemoglobin was 11.3 grams and remained at about this level until his discharge from the hospital on January 8, when it was 10.8 grams. Because of the complete absence of clinical icterus following the second exchange transfusion, no further serum bilirubin measurements were performed. Examination of the baby on the day of discharge was entirely normal. He was vigorous and gaining well despite some watery stools. He was discharged home on a Dryco and water formula with supplements of strained meat, iron, and vitamins and was followed in my private office.

During his office visits, hemoglobin and reticulocyte count determinations were performed and their values are depicted in Fig. 1. From the time of discharge from the hospital to the present time, he has gained weight well and shown no signs of serious illness. Nevertheless, his hemoglobin values continued to drop and there were no reticulocytes demonstrated in the peripheral blood smear. When the hemoglobin reached a low level of 8.4 grams on January 16, with still no reticulocyte response, I elected to attempt to stimulate the bone marrow by the use of cortisone. Oral therapy was begun with 25 mg. every six hours and continued in decreasing amounts until March 2, when it was discontinued. The total amount of cortisone given was 1,800 mg. There was an immediate reticulocyte increase to 0.2 per cent on January 19 and 19 per cent on January 22. The hemoglobin rose to 12.8 grams on March 2, when it was discontinued. A two-month follow-up check has demonstrated continued normal hemoglobin values. A bone marrow study on February 9 was performed

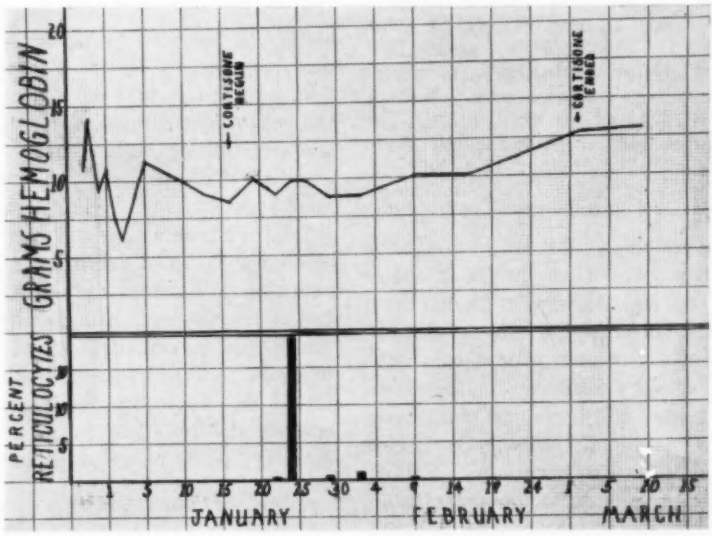

Fig. 1.

by Dr. Arthur Seaman of the University of Oregon Medical School from a tibial tubercle sample. He reported a highly cellular marrow with active leukopoiesis, thrombocytopoiesis, and erythropoiesis.

A study of the family's blood genotype by Dr. Arthur Frisch of the University of Oregon Medical School revealed the patient to be Group "A," type N DcE (Rh-positive subtype Rh_2); the mother, Group "O," type Mn dee (Rh negative), and the father, Group "A," type Mn DcE (Rh positive, subtype Rh_2). The following titrations were performed on the mother's sera using Rh_1 and Rh_2 cells: Feb. 2, 1953—Rh antibodies, none; anti-A antibodies, 1:4096. March 9, 1953—Saline antibodies, none; albumin antibodies, none; Coombs' antibodies, none; anti-A titer, 1:1024; anti-B titer, 1:128. The maximum normal titer for anti-A in Dr. Frisch's laboratory is 1:256.

DISCUSSION

This case demonstrates the confusion that may arise when, in the presence of an obvious hemolytic disease in a newborn infant, the direct Coombs test is negative and no maternal anti-Rh antibodies can be demonstrated. In this case, one exchange transfusion failed to stop the hemolytic disease and another was necessary. Following the second exchange transfusion, all evidence of icterus disappeared, but a marked anemia continued. From this time the problem was no longer one of excessive blood destruction, but of failure of erythrocyte regeneration.

Diamond and associates[5] have described a relative hypoplasia of the bone marrow in severe erythroblastosis fetalis following exchange transfusions. It is possible that spontaneous regeneration of the erythrocytes would have occurred eventually had cortisone not been used. The decision to use cortisone therapy was reached because of the recent favorable reports of hormone therapy in refractory anemias[6] and because of the author's favorable experience in observation of cortisone used in a case of congenital hypoplastic anemia.[7]

The results were gratifying as evidenced by the rise in hemoglobin, the increase in reticulocytes, and the microscopic appearance of the bone marrow following its use.

Hypoplasia of the bone marrow following erythroblastosis fetalis associated with isoimmunization of the mother by the fetal agglutinogen "A" was described by Smith[8] in 1949. Certain similarities between his case and the case under discussion are the high maternal anti-A serum titers and the negative Coombs test. Erythrocyte aregeneration was of considerable duration in Smith's case and was treated by repeated blood transfusion. It is tempting to surmise the effect of cortisone in his case, had it been used. Smith postulated that prolonged depression in erythropoiesis may result from an antibody directed solely against the red cells in fetal life or from the early neonatal period.

CONCLUSIONS

1. A case is presented of a newborn infant who developed aregenerative anemia following successful treatment of erythroblastosis fetalis due to isoimmunization of the mother by the fetal blood agglutinogen "A."

2. There was prompt red blood cell regeneration after the use of oral cortisone.

REFERENCES

1. Polayes, S. H.: Erythroblastosis Fetalis in Mothers With Rh-positive Blood. Report of Six Cases, With Comment on Iso-

immunization With the "A" and "B" Agglutinogens, Am. J. Dis. Child. 69: 99, 1945.

2. Polayes, S. H., and Ohlbaum, C.: Erythroblastosis Fetalis Unrelated to the Rh Factor; Report of Cases Suggesting Isoimmunization of Group "O" Mothers by "A" Children, Am. J. Clin. Path. 15: 467, 1945.
3. Polayes, S. H., and McNally, J., Jr.: Isoimmunization With the A and B Factors and Its Relation to Hemolytic Disease of the Newborn, Am. J. Clin. Path. 18: 375, 1948.
4. Orozco, A. C. V.: The A and B Factors as a Possible Cause of Erythroblastosis, Blood, Special Issue No. 2, The Rh Factor, p. 164, Jan., 1948.
5. Diamond, L. K., Allen, F. H., Vann, D. D., and Power, J. R.: Round-table Discussion of Erythroblastosis Fetalis, Pediatrics 10: 337, 1950.
6. Hill, J. M., and Hunter, R. B.: ACTH Therapy in Refractory Anemias, Proc. Second Clinical ACTH Conference, vol. 11, p. 181.
7. Seaman, A. J.: Cobalt and Cortisone Therapy in Chronic Erythrocytic Hypoplasia, Am. J. Med. 13: 99, 1952.
8. Smith, C. H.: Chronic Congenital Aregenerative Anemia (Pure Red-Cell Anemia) Associated With Iso-Immunization by the Blood Group Factor "A," Blood 4: 697, 1949.

CHRONIC LOW-LEVEL EXPOSURES OF YOUNG MICE TO IONIZING RADIATIONS AND THE EFFECT ON FERTILITY

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IONIZING radiations have frequently been used to produce sterility. Low-level single exposures to the rabbit[21] or chronic low-level exposures to the rat, rabbit, or dog[17] have been shown to have a cumulative effect toward sterility. Eschenbrenner and his colleagues[4-8] maintained that the testes is so radiosensitive that it can be used as a fairly reliable dosimeter. Recently Neary and associates[22] found that fast neutrons caused sterility in male mice more readily than in females, a situation diametrically opposed to the effects of gamma or x-rays. Ovarian tumors have been produced by low-level exposures.[28] There are certainly genetic effects at low levels of exposure of the gonads.[2, 3, 9, 13, 16, 23, 27, 29] and Muller[19, 20] is convinced that a single ionization may cause a mutation in a gamete. Within the tolerance range of whole body exposure to ionizing radiations, there may be a mutational change at the lowest and complete sterility at the highest level.

There have been no systematic studies on fertility of mice exposed chronically to ionizing radiations from the time of weaning through the normal reproductive period and tested periodically for fertility. This study was planned to determine the effect on fertility of weekly injections of radioiodine (NaI^{131}) which emits both beta and gamma radiations, but which tends to concentrate in the thyroid gland, and parallel exposures to x-rays of both male and female mice beginning at 2 months and continuing through the normal reproductive period to one year of age.

MATERIALS AND METHOD

The 225 mice used in this study were of the Swiss albino stock raised in our laboratory. They were recently weaned animals at the beginning of the study, and each animal was individually earmarked for identification.

Beginning at 7 weeks of age the mice were treated each Friday for a continuous period of forty-four weeks so that they were approximately 12 months of age at the termination of the study. The normal reproductive span of these mice is shortly after weaning to more than one year of age, although the termination of reproductive activity for any particular mouse may extend to 15 months. Since this study was terminated when the mice were 12 months of age, the factor of natural reproductive senility was not involved.

The treatment of the mice is shown in Table I.

The x-irradiated mice were exposed five at a time in a circular plastic con-

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tainer with inside dimensions as follows: diameter 15 cm., height 4 cm. The ionization chamber used to determine skin dosage was placed in the center of this cage at the level of the center of the body of each mouse. The physical constants were: Westinghouse Quadrocondex Constant Potential Therapy X-ray Machine run at 210 KVP, 15 Ma., filtration 0.28 Cu and 0.50 Al, target distance 50 cm., and air dose rate of 96.2 r. per minute. The exposure time was 6.24 seconds for 10 r. Since the output of the machine was brought to full capacity before the shutter was tripped, the mice received exactly 10 r. at weekly intervals. This dose of 10 r. was arbitrarily chosen as one which might prove to be comparable in effect to an injection of 4 μc per week of radioiodine. There is no really accurate method of equating biologically the x-rays and the beta and gamma rays from radioiodine.

The radioiodine was received weekly from the Pile at Oak Ridge in the form of carrier-free NaI^{131} and was diluted so that each cubic centimeter contained 4 μc of the isotope. Following injection of all mice receiving this largest injection of 4 μc, the remaining I^{131} was diluted with an equal volume of distilled water so that the new concentration was 2 μc per cubic centimeter. In this way an equivalent volume of fluid was injected into each mouse but the concentration of radioiodine varied from 4 down to 1 μc per cubic centimeter. The doses of I^{131} chosen were based upon previous experience of tolerable but damaging levels.[25]

The control mice received a similar volume (1 c.c.) of a solution of elementary iodine in distilled water. This iodine is nonradioactive and was made up in a concentration of 5×10^{-8} gamma per cubic centimeter which represented a concentration comparable to the level of iodine injected into the 4 μc I^{131} mice. In this way there was a check on the effect of iodine per se, apart from the radioactive emanations from the I^{131}.

TABLE I

WEEKLY TREATMENT	MALES	FEMALES	TOTAL	
Controls: Injecetd with nonradioactive, elementary iodine	12	13	25	(21)
Exposure to 10 r. whole body x-rays	21	19	40	(34)
Injection with radioiodine				
1 μc	17	23	40	(31)
2 μc	26	24	50	(34)
4 μc	28	42	70	(58)
Totals	104	121	225	(178)

Note: Figures in parentheses refer to the number of survivors at the termination of the study. The greatest mortality occurred among the radioiodine-injected mice (32%) as compared with a figure of 16% for the controls.

The mice were all kept in groups of five in regulation stainless steel cages with food and water ad libitum. The room temperature was maintained at 72° F. throughout the entire experiment. Aside from the planned fertility tests, none of the experimental animals was allowed to mate.

The fertility tests were made eleven times at four-week intervals for a total of forty-four weeks. To test every animal for fertility would not only remove some 208 females and 121 males

from stock each four weeks, but would use an additional 329 cages. From a statistical point of view such a complete record was not necessary. Therefore, at four-week intervals at least two males and four females were selected at random from each of the five categories of treatment. No mice were retested until all others, similarly treated, had been tested. At the termination of the experiment all the surviving mice were tested for fertility. The males were placed each with two normal stock females which were known to be fertile by virtue of a previous normal pregnancy. The males to be tested were left with the two females for six days, since the mouse is known to have a five-day estrus cycle. The females to be tested were each given a previously tested male for a period of six days. Matings were always begun on a Monday since this would provide a three-day lapse of time following the previous Friday injection with I^{131} and there could be little or no contamination effect on the normal stock animal being used for the fertility test.

At the termination of the experiment the thyroid, pituitary and adrenal glands, the spleen, gonads, and limb bones were all preserved for histological study. Since this report deals with the fertility-sterility factor, it will include only the histopathological findings of the gonads along with the fertility-sterility data.

OBSERVATIONS AND EXPERIMENTAL DATA

In fertility tests extending over a period of ten months, we are dealing with several possible factors:

(1) Initial sterility followed by the possible "recovery" of fertility.

(2) Delayed sterility, due to differential damage to germ cells at different stages of maturation. This may be transient or permanent.

(3) Immediate and permanent sterility.

Table II summarizes the results of the fertility tests made at intervals of four weeks throughout the experimental period of forty-four weeks. It also gives the over-all results which indicate a definite reduction in fertility of the female mice x-rayed or receiving injections of radioiodine. Fertility of the x-rayed females was reduced to zero by thirty-two weeks. The larger dose of radioiodine (4 μc per week) did not cause such complete sterility but did reduce the fertility from 73 per cent, found in the controls, to 47 per cent for the entire experimental period of forty-four weeks. The over-all reduction in fertility of the x-rayed females was to 22 per cent, but if one examines Table II for progressive changes it will be seen that by twenty weeks (fifth test period) sterility in the female was almost complete. This means that an accumulated exposure of only 200 r. given in 10 r. weekly doses seemed to be sufficient to cause sterility in the female for whom the exposure began at 7 weeks of age, even though this dose was fractionated over a period of twenty weeks. The highest injection of radioiodine (i.e., 4 μc per week) never caused this degree of sterility, although it did reduce fertility to 38 per cent by the end of the experimental period. The effect of this level of radioiodine on female fertility was first manifest at about the seventh test period or twenty-eight weeks following initiation of treatment. This value of 38 per cent should be compared with 67 per cent for the

controls, which group also showed a drop in fertility. Whether this was due to age or to environmental factors cannot be stated although we can be assured that the conditions were the same for the experimental and the control mice.

In none of the experimental males, whether treated with x-rays or with reproductive capacities and under the conditions described.

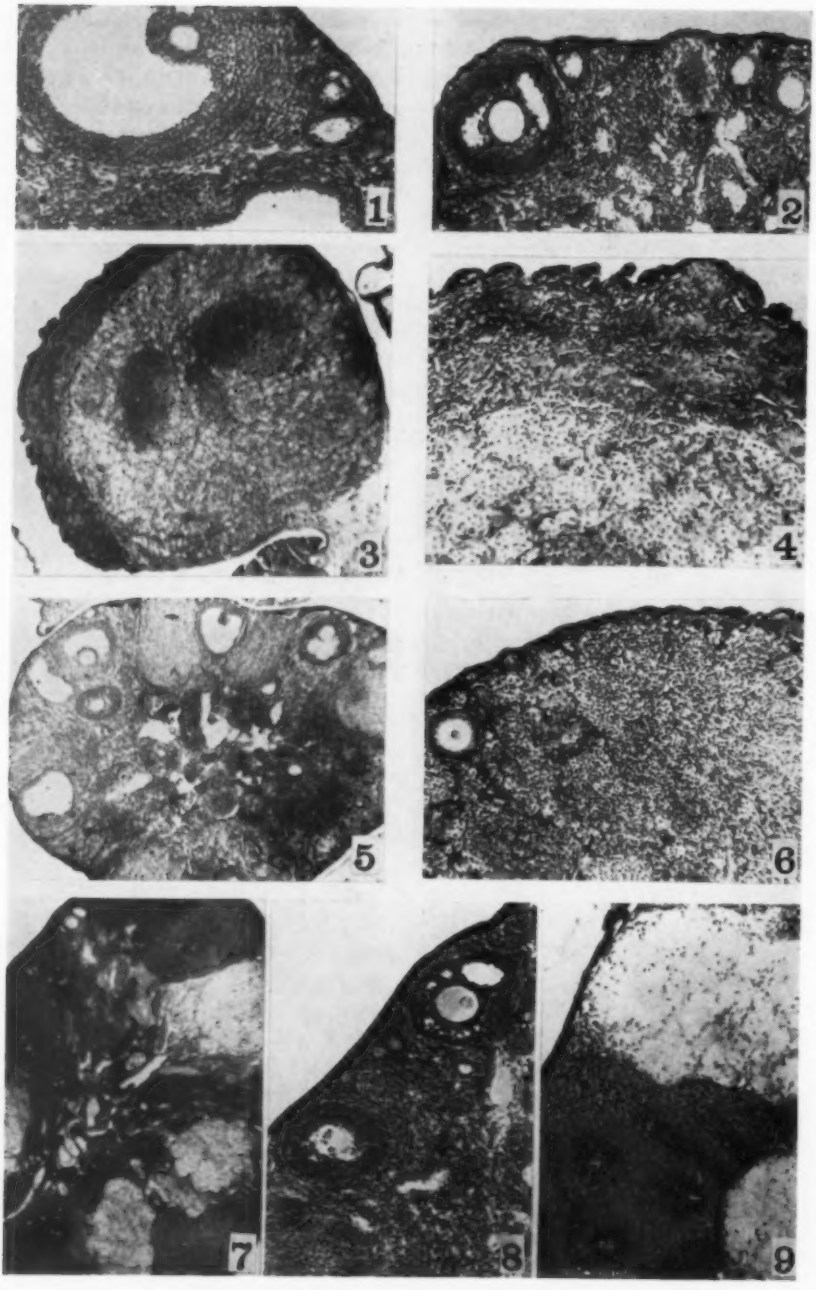
The histological study of the gonads showed no effect in any of the testes, all having the full complement of seminiferous tubules filled with the normal maturation stages. The control ovary had abundant follicles and the normal number of corpora lutea with no evi-

TABLE II

4-WEEK TEST PERIODS	CONTROLS			X-RAYED (10 R.)			RADIOIODINE 1 μc			2 μc			4 μc			MONTH
	+	−	%	+	−	%	+	−	%	+	−	%	+	−	%	
Fertility Tests: Males																
1	18	2	90	2	0	100	2	0	100	2	0	100	2	0	100	April
2	2	0	100	2	0	100	2	0	100	2	0	100	2	0	100	May
3	2	0	100	2	0	100	2	0	100	2	0	100	1	1	50	June
4	2	0	100	2	0	100	2	0	100	2	0	100	2	0	100	July
5	2	0	100	0	2	0	1	1	50	1	1	50	1	1	50	Aug.
6	2	0	100	2	0	100	2	0	100	1	1	50	2	0	100	Sept.
7	2	0	100	2	0	100	2	0	100	1	1	50	2	0	100	Oct.
8	1	1	50	2	0	100	1	1	50	2	0	100	2	0	100	Nov.
9	1	1	50	2	0	100	2	0	100	1	1	50	2	0	100	Dec.
10	4	0	100	8	0	100	5	0	100	5	3	60	4	3	56	Jan.
11	5	0	100	8	0	100	6	0	100	6	0	100	10	0	100	Feb.
Total tests	41	4	91	32	2	94	27	2	93	25	7	78	30	5	86	
Fertility Tests: Females																
1	5	0	100	3	1	75	1	1	50	3	1	75	3	1	75	April
2	10	0	100	2	3	40	5	0	100	2	3	40	0	5	0	May
3	3	0	100	1	4	20	0	5	0	0	5	0	1	3	25	June
4	2	3	40	5	0	100	4	1	80	3	2	60	4	0	100	July
5	5	0	100	0	5	0	5	0	100	2	2	50	5	0	100	Aug.
6	0	4	0	0	5	0	0	4	0	4	1	80	4	1	80	Sept.
7	2	1	67	2	3	40	4	1	80	1	3	25	3	2	60	Oct.
8	3	2	60	0	5	0	2	3	40	1	4	20	2	3	40	Nov.
9	4	0	100	0	4	0	4	1	80	2	2	50	1	3	25	Dec.
10	2	3	40	0	7	0	3	2	60	8	4	67	6	12	33	Jan.
11	4	2	67	0	8	0	10	4	70	5	3	60	7	11	38	Feb.
Total tests	40	15	73	13	45	22	38	22	63	31	30	51	36	41	47	

the various injections of radioiodine, was fertility reduced below 78 per cent for the over-all period. Since every surviving male was found to be 100 per cent fertile in the tests at the termination of the experiment (at 44 weeks of age), it must be concluded that the male is much more radioresistant to beta, x, and gamma rays than is the female with respect to its

dence of senile degeneration at 51 weeks of age (Figs. 1 and 2). The ovaries of mice exposed to 10 r. x-rays each week for a total accumulated dose of 440 r. x-rays over forty-four weeks showed no follicles at any level of section (Figs. 3 and 4). The ovaries were reduced in size, appeared to be fibrotic, and very compact with thickened cortex. There was some periph-



Figs. 1-9.—*(For legends see opposite page.)*

eral vascularization. The medullary portion appeared to be made up of columns of cells simulating embryonic sex cords without any evidence of follicular structure. These ovaries had all produced viable ova so that the histological picture was definitely one of radiogenic degeneration.

The ovaries of females subjected to weekly radioiodine injection showed variable histological pictures (Figs. 5 and 6). Every ovary contained some quite normal-appearing follicles. At the higher level of treatment (4 μc I^{131} per week) there appeared to be some anovular areas and some degeneration. The number of normal follicles was definitely reduced. In some there appeared edematous areas, but no evidence of hyperemia (Figs. 7 to 9). The cortex was not particularly thickened. One would classify these ovaries as affected but definitely not sterile. This was confirmed in the previously reported fertility tests. Histologically, 10 r. x-rays each week were far more damaging to the female than was 4 μc I^{131}.

DISCUSSION

Since the radioactive isotope I^{131} had an 8-day half-mile of radioactivity and since it was injected every seven days for the duration of the experiment, it was calculated that a maximum base line of accumulated (residual plus injected) radioactivity of 1.76 μc was concentrated largely in the thyroid glands of the mice injected with 4 μc per week.[25] This peak was reached in about four weeks following initiation of the experiment, and was maintained throughout. For the 2 μc level of injection the peak was 0.88 μc, and for the 1 μc level of injection it was 0.44 μc base plateau of concentration. These estimates are entirely theoretical since actual counter measurements could not be taken, and they are therefore subject to wide physiological (biological) variations. This takes into account, however, the known excretion rate of I^{131} of about 80 per cent[24] which occurs within the first twenty-four hours following injection, in addition to the known decay rate.

It must be pointed out that the term "chronic" is not exactly descriptive of the conditions outlined in this experiment. There was no constant exposure to a constant level of ionizing radiations. However, the animals treated with radioiodine were subjected to a constant base level exposure of ionizing beta and gamma radiations. However, the actual level varied from a maximum at the moment of injection to a minimum at the moment (the base plateau) before the next weekly injection. Since the radioiodine is very rapidly excreted, it is assumed that the "chronic" or "constant" level of exposure is represented by the lower figure given as the base plateau above.

Figs. 1 and 2.—Cortical region of normal, control ovary of 1-year-old mouse.

Fig. 3.—Ovary of mouse at one year following whole body exposure to 10 r. x-rays weekly for forty-four weeks. Note complete absence of follicles, thickening of cortex, and fibrosis of medullary portion.

Fig. 4.—Enlarged portion of Fig. 3. Note same hyperemia.

Fig. 5.—Ovary of mouse at one year following injection of 4 μc I^{131} weekly for forty-four weeks. Note normal topography, maturing follicles, and corpora lutea.

Fig. 6.—Enlarged view of Fig. 5 at region where the cortex is devoid of follicles and the ovarian stroma appears to be made up of cordlike masses of cells resembling sex cords of the differentiating gonad.

Figs. 7 to 9.—Ovary of female at one year injected weekly with 2 μc I^{131} for forty-four weeks, showing evidence of edema and possible early neoplasia. Some quite normal follicles and corpora lutea evident.

In the case of the radioiodine-treated mice there was therefore a surge of exposure immediately after injection, which level declined to the base plateau, probably approaching it within a little more than twenty-four hours. Further, since the thyroid gland has a particular avidity for iodine, this isotope is rapidly concentrated in that endocrine gland so that exposure of the body as a whole or the gonads in particular is very much reduced. The presumption that the presence of radioiodine in the body of the female does bring on a degree of sterility seems to be adequately substantiated.[25, 23] However, the method or pathway of such sterilization is not yet determined. Very little of this radioiodine is found in the ovary itself, but a considerable amount remains in the skin and carcass.[24] Some 77 per cent is concentrated in the thyroid gland which is rapidly ablated following certain high levels of injection.[24] Whether it is the direct ovarian concentration, or the thyroid damage which secondarily affects the gonads, or both factors, one cannot state definitely at this time. Some investigators are tempted to suggest that the internal location of the ovary might make it more subject to the gamma emanations from the thyroid-concentrated radioiodine than would be the condition for the more distally located testes of the male. The testes at 4 μc per week of I^{131} do not show any appreciable reduction in fertility nor histological evidence of destruction. However, recent evidence[26] indicates that the thyroid gland of the female mouse is adversely affected to a degree somewhat more than is the thyroid gland of the male when the animals are injected with similar doses of radioiodine. Therefore, the suggestion that the ovary is affected by way of the thyroid gland cannot be ruled out.

We are still faced with the data on whole body x-irradiation which indicates a very great differential in susceptibility of the ovary over the testis. The male mice terminated the experiment with an accumulated 440 r. x-rays with no reduction in fertility whatsoever, while the females showed almost complete sterility as early as the fifth test period (twenty weeks or 200 r. accumulated). If the biological effect of ionizing radiations from radioiodine and from x-irradiations are comparable, one would have to admit that for the ovary 10 r. per week x-rays are more damaging than is 4 μc per week of I^{131}, and that either is more damaging to the ovary than to the testis. One still cannot be certain of the manner of the effect of ionizing radiations on the mouse gonads, although the effect is definite and is differentially adverse for the ovary as compared to the testis.

In analyzing the fertility data one must admit that monthly sampling might not be as accurate as periodic tests of all experimental animals. Nevertheless, continuous fertility tests of the same animal might introduce a factor of reproductive fatigue which is not of interest in this study. If one evaluates the data as suggestive, month by month, and indicative, for the over-all picture, the method used here seems to be sufficiently valid. It should be noted, for instance, that even the control females showed low fertility at the sixth test, as did some of the experimentals. This might well be attributed to a seasonal low in reproductive activity in September. The "over-all" fertility is simply the summation of fertility tests for the period of the study and, except possibly for the x-rayed

females which quickly became sterile, these figures seem of real indicative value. An independent consideration is the final fertility of all survivors, and these data are directly comparable. Here, too, one might be tempted to question the value of the data since it does not take into consideration the factor of lethality. However, as indicated, the death rate among the experimental mice was not appreciably different from that for the controls, so that possibly the terminal fertility tests are the most significant.

There have been numerous reports of radiation-induced ovarian tumors in mice.[10, 11, 12, 14, 15] Whole body exposures or spot irradiation of the ovaries resulted in degeneration of the follicles by seven to eight weeks and then there often developed proliferative changes in the germinal epithelium which resulted in the development of tumorous growths. These were sometimes tubular adenomas, granulosa-cell tumors, or luteomas.[28] The granulosa-cell tumors were the most common in mice and, according to Speert, are similar histologically to those that occur in human beings. There is evidence of estrogenic activity of these ovaries. The tumors are transplantable and are known to metastasize. The luteomas are benign and Speert believes them to be due to a hormonal disturbance, resulting from a suppression of the production of estrogens. This may be the mechanism by which radiations cause tumor development. The ovaries in this series were not positively tumorous but, particularly in the x-rayed mice, the ovaries did present areas of neoplastic-like growths. Very possibly if such mice had been allowed to live to 15 months or more the ovaries of the x-rayed animals might well have become tumorous. This statement is based upon the histological picture at one year of age, and when compared with the ovary of the normal control of the same age.

SUMMARY AND CONCLUSIONS

1. Some 225 mice were exposed to low weekly doses of x-rays or radioiodine (subcutaneous injection) for forty-four weeks, beginning at the time of weaning (7 weeks of age), and were sample tested at monthly intervals for fertility. At the termination of the experiment, all gonads were examined histologically.

2. The experimental mice (200) survived the duration almost as well (79 per cent) as did the controls (84 per cent). The highest mortality (32 per cent) occurred among those mice receiving weekly injections of 2 μc of I^{131} (not 4 μc).

3. None of the males showed a statistically significant drop in fertility when compared with the controls. This statement applies equally to those exposed to weekly doses of 10 r. x-rays (aggregate 440 r.) or to 4 μc of I^{131} (aggregate 176 μc of I^{131}). All surviving males tested at the termination of the experiment were fertile.

4. The females in all categories, controls and experimentals, showed a drop in fertility when compared with males —either over-all fertility or fertility with progressive time.

5. Radioiodine at the dose levels used was not sterilizing with respect to the ovary although with increasing doses there was a lowering of fertility. The over-all fertility of 4 μc of I^{131} females was 47 per cent as compared with 73 per cent for the controls. The histological analysis of these ovaries showed a wide range of response, some appearing quite normal (even at 4 μc

of I^{131} per week) and others (even at 2 μc of I^{131} per week) developing large edematous areas, anovular cortices, and early evidence of neoplasias. Every ovary had some normal follicles, and most ovaries showed some areas of histological damage.

6. Whole body x-irradiation to 10 r. per week for forty-four weeks produced completely sterile ovaries in every instance. There was no evidence of any follicles anywhere and the cortex was thickened and pigmented while the stroma (medulla) appeared fibrotic and made up of columns of cells simulating the sex cord cells of the differentiating gonad.

7. The female mice receiving 10 r. whole body x-radiation weekly were completely sterilized after the seventh month or following an accumulated exposure of 280 r. x-rays. Many were sterile at an earlier stage (i.e., fifth month following 200 r. x-rays). The over-all fertility (fertility tests of all females over the 11 months) was 22 per cent as compared with 73 for the controls.

8. One must conclude from such a study as this that beta, gamma, and x-rays are more damaging to the ovary than to the testes; that 10 r. x-rays are more deleterious than 4 μc of I^{131} given weekly; and that when given at weekly intervals an accumulated dose of 280 r. x-rays appeared to be completely sterilizing for the female mouse, while 440 r. of x-rays over forty-four weeks did not appreciably reduce male fertility.

REFERENCES

1. Bali, T., and Furth, J.: Morphological and Biological Characteristics of X-ray Induced Transplanted Ovarian Tumors, Cancer Res. **9**: 449, 1949.
2. Burgher, J. C.: Delayed Radiation Effects at Hiroshima and Nagasaki, Nucleonics **10**: 18, 1952.
3. Ellis, F.: The Genetic Effects of Non-sterilizing Doses of Penetrating Radiations, Brit. J. Radiol. **21**: 1, 1948.
4. Eschenbrenner, A. B., Miller, E., and Lorenz, E.: Quantitative Histologic Analysis of the Effect of Chronic Whole-body Irradiation With Gamma Rays on the Spermatogenetic Elements and the Interstitial Tissue of the Testes of Mice, J. Nat. Cancer Inst. **9**: 133, 1948.
5. Eschenbrenner, A. B., and Miller, E.: Quantitative Histologic Analysis of the Testes of Mice Following a Single Total Body Exposure to X-rays, ANL **4451**: 42, 1950.
6. Eschenbrenner, A. B., and Miller, E.: Quantitative Histologic Studies of the Testes of Mice Exposed to 50 r X-rays, ANL **4531**: 17, 1950.
7. Eschenbrenner, A. B., and Miller, E.: Effect of Roentgen Rays on the Testis: Quantitative Histological Analysis Following Whole Body Exposure, Arch. Path. **50**: 736, 1950.
8. Eschenbrenner, A. B., Wang, T., and Miller, E.: The Value of Mouse Testes for Biological Dosimetry of Ionizing Radiations, ANL **4451**: 39, 1950.
9. Evans, R. D.: Quantitative Inferences Concerning the Genetic Effects of Radiations, Science **109**: 299, 1949.
10. Furth, J.: Relation of Pregnancies to Induction of Ovarian Tumors by X-rays, Proc. Soc. Exper. Biol. & Med. **71**: 247, 1949.
11. Furth, J., and Bonn, M. C.: Induction of Ovarian Tumors in Mice by X-rays, Cancer Res. **7**: 241, 1947.
12. Gardner, W. U.: Ovarian and Lymphoid Tumors in Female Mice Subsequent to Roentgen-ray Irradiation and Hormone Treatment, Proc. Soc. Exper. Biol. & Med. **75**: 434, 1950.
13. Howard, A.: Radiation Genetics. I. Genetic Aspects of Radiation Risks, Brit. J. Radiol. **25**: 177, 1952.
14. Kaplan, H. S.: Influence of Ovarian Function on Incidence of Radiation-induced Tumors in Mice, J. Nat. Cancer Inst. **11**: 125, 1950.
15. Li, M. H., and Gardner, W. U.: Further Studies on the Pathogenesis of Ovarian Tumors in Mice, Cancer Res. **9**: 35, 1949.
16. Lorenz, E.: Some Biologic Effects of Long Continued Irradiation, Am. J. Roentgen. **63**: 176, 1950.
17. Metcalf, R. G., and Inda, F. A.: Pathology in Animals Subjected to Repeated Daily Exposure to Roentgen Rays, UR-88, 1951, University of Rochester.
18. Muller, H. J.: Is Irradiation a Menace to Posterity? Science News Letter, June 11, 1949.
19. Muller, H. J.: Radiation Damage to the Genetic Material, Am. Scientist **38**: 33, 1950.

20. Muller, H. J.: Some Present Problems in the Genetic Effects of Radiation, J. Cell. & Comp. Physiol. **35**: 9, 1950.
21. Murphee, R. L., Whitaker, W. M., Wilding, J. L., and Rust, J. H.: Effects of Whole Body Exposure Upon Subsequent Fertility of Male Rabbits, Science **115**: 709, 1952.
22. Neary, G. J., Munson, R. J., and Mole, R. H.: Effects of Daily Irradiation by Fast Neutrons on Male Fertility, Nature **171**: 256, 1953.
23. Plough, H. H.: Radiation Tolerance and Genetic Effects, Nucleonics **10**: 16, 1952.
24. Rugh, R.: The Mouse Thyroid and Radioactive Iodine (I^{131}), J. Morphol. **89**: 323, 467, 1951.
25. Rugh, R.: The Effect on the Thyroid Gland and the Gonads Following Chronic Treatment of Mice With Low Doses of Radioiodine I^{131}, J. Exper. Zool. **122**: 151, 1953.
26. Rugh, R.: Selective Sterilization of Young Female Mice by Radioiodine Transmitted Through the Mother's Milk, Proc. Soc. Exper. Biol. & Med. **83**: 762, 1953.
27. Russell, W. L.: Mammalian Radiation Genetics, Symposium on Radiobiology, National Academy of Science, 1952.
28. Speert, H., Quimby, E. H., and Werner, S. C.: Radioiodine Uptake by the Fetal Mouse Thyroid and Resultant Effect on Later Life, Surg., Gynec. & Obst. **93**: 230, 1951.
29. Uphoff, D. E., and Stern, C.: The Genetic Effects of Low Intensity Irradiation, UCRL-255, 1948, University of California Radiation Laboratory.

SKIN CARE OF THE NEWBORN INFANT

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RECENT years have seen the elimination of many of the meddlesome procedures long regarded as sacred to the care of the newborn infant. His mouth, ears, and nostrils are no longer subject to traumatic cleansing by gauze or swab. More recently[1, 2] baths and inunctions have been rather generally discarded in favor of "dry care." This technique permits the coating of vernix caseosa to remain on the skin except for the initial removal of blood and debris from the face and scalp. Subsequent care of the diaper area varies, tap water, sterile water, baby oil, or lotion being used for the removal of fecal soil. Skin folds are cleansed with water, oil, alcohol, or are left alone. Advocates of dry care suggest that the vernix acts as a sort of protective vanishing cream, and that by leaving it intact, microscopic abrasions and contamination incident to its removal are avoided. In addition, opportunities for cross-infection are reduced by obviating the need for a common bath slab. This type of skin care has proved quite satisfactory and has been widely adopted.

At the St. Louis Maternity Hospital, dry care was adopted in 1940 and was used exclusively in the five nurseries of the hospital for about nine years, employing the following routine:

(1) Removal of blood and vernix from the head and face in the delivery room, using warm oil.

(2) A shampoo with soap and water, and removal of any remaining vernix from the creases with a moist cotton ball at twenty-four hours.

(3) Subsequent to this, regardless of length of hospitalization, an "inspection bath," plus cleansing of the diaper area with cotton balls moistened in water. Theoretically, an "inspection bath" consists of removal of visible debris with a moist cotton ball.

No true epidemics of impetigo neonatorum occurred during this period, yet sporadic cases were not infrequent, as shown in Fig. 1. Only through early detection, immediate isolation, and prompt treatment could this nursery bugaboo be kept at merely a nuisance level. That impetigo is still a potential menace to the newborn despite antibiotics (or perhaps bearing a relation to strains of bacteria resistant to these drugs) is dramatically illustrated by the experience of Lee and associates[3] who reported a biphasic epidemic which occurred in 1948, with twelve cases of uncomplicated impetigo and ten cases of Ritter's disease, the latter carrying a 50 per cent mortality. That superior nursery technique may still not offer adequate protection was recently shown by Farquharson and co-workers[4] who found that they were unable to rid their nurseries of the ubiquitous

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Aided by a grant from Winthrop-Stearns, Inc.

staphylococcus by any means at their disposal. They were, however, able to reduce the incidence of impetigo neonatorum from 6.54 to 0.63 per cent by the introduction of pHisoHex baths for the infants, beginning twenty-four hours after delivery and repeated every other day during the infant's stay.

In February of 1949, we instituted the pHisoHex* (pHisoderm reinforced with 3 per cent hexachlorophene) hand scrub for all nursery personnel and physicians examining newborn babies. Numerous reports[5, 6, 7] suggest the superiority of this product to the usual soap scrubs with respect to: (1) effective bacteriostasis, which is cumulative in action if pHisoHex is used repeatedly and exclusively for scrubs, (2) reduction in time necessary for an adequate scrub, (3) greatly decreased incidence of skin irritation of the hands.

The pHisoHex scrub was accepted enthusiastically by the nursery personnel who perform as many as two hundred hand washings per individual eight-hour shift. Because there was less chapping and soreness, it was felt that hand washing was more conscientiously carried out than before. This new scrub technique was not in itself the solution to our problem, however, since the incidence of impetigo was at its peak in that year (2.00 per cent of 3,189 live births). We were very dissatisfied with this incidence, which in terms of actual cases meant six to seven infected babies every month.

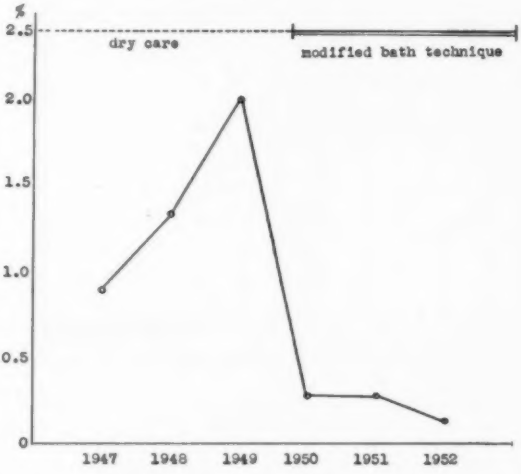
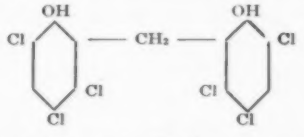


Fig. 1.—Incidence of impetigo neonatorum, 1947 to 1952 (per cent of living births).

*pHisoHex is basically a synthetic, sudsing, skin detergent composed of sodium octylphenoxyethoxyethyl ether sulfonate, lanolin cholesterols, and petrolatum, to which is added 3 per cent hexachlorophene ("G-11") having the chemical composition 2,2'-dihydroxy 3,5,6-3',5',6'-hexachlorodiphenylmethane:



It is manufactured by Winthrop-Stearns, Inc., New York.

During the summer of 1949, therefore, we decided to make a radical change in our skin care, and over a period of several months one group of babies was continued on the usual dry care, and a second group was given pHisoderm* (oily) baths according to the following plan:

(1) The face and scalp are cleansed of blood and vernix in the usual manner in the delivery room.

(2) On the third day of life (counting the day of birth as the first day) and every other day thereafter, a spray bath employing pHisoderm (oily) is given. This is done in the following manner:

(a) Cover the bath slab with a large (24 × 16 in.) quilted pad.

(b) Place the infant nude on the pad and cover the cord stump with a gauze flat soaked with 70 per cent alcohol.

(c) Using an ordinary spray nozzle attachment, wet the baby, avoiding the cord region insofar as possible.

(d) Pour a few cubic centimeters of pHisoderm in the hands and lather the infant's body with the hands, covering the diaper area last.

(e) Spray off the pHisoderm following the same pattern.

(f) Move the infant to his own crib and gently pat the skin dry.

This proved so successful that in September, 1949, we abandoned dry care in the four nurseries accommodating full-term babies. It is still used in the Premature Nursery where the babies are bathed only on special order. The immediate reduction in impetigo in 1949 is seen in Fig. 2. The incidence of impetigo dropped from 2.00 per cent in 1949 to 0.29 per cent in 1950 and 1951, and to 0.13 per cent in 1952, as is seen by referring back to Fig. 1.

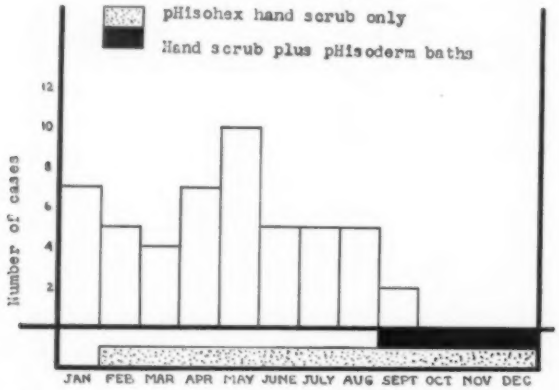


Fig. 2.—Incidence of impetigo neonatorum by month, 1949, in relation to initiation of pHisoHex hand scrub and pHisoderm bath.

It was interesting that in spite of the extra work for the nursery attendants, entailed by the spray baths as compared with the inspection baths, the girls were universally in favor of the change, not only because of fewer skin troubles but because the babies were "really clean." Minor skin irritations also have been markedly reduced with the pHisoderm baths. Erythema toxicum, or newborn rash, is unaffected. pHisoderm (oily) is ap-

*pHisoderm is the detergent previously mentioned but without added hexachlorophene. pHisoderm (oily) contains a higher percentage of emollients than pHisoderm (regular) or pHisoHex.

parently a benign hypoallergenic substance. We have not seen contact dermatitis following its use.

DISCUSSION

It has been a matter of interest to us that dry care, so universally accepted, has been less satisfactory in our experience than a return to the baby bath, using a sudsing detergent especially suited to the newborn skin. Several factors may be related to this observation.

mother is less easily understood. Although we have never found any completely satisfactory explanation for this observation, we presume it may be associated with the longer hospital stay of the private group, which in our hospital is still ten days. Mothers on ward status leave on the seventh or sixth post-partum day unless the need for beds is so urgent that they are discharged even earlier. It has been suggested that the skin of the newborn infant is relatively sterile

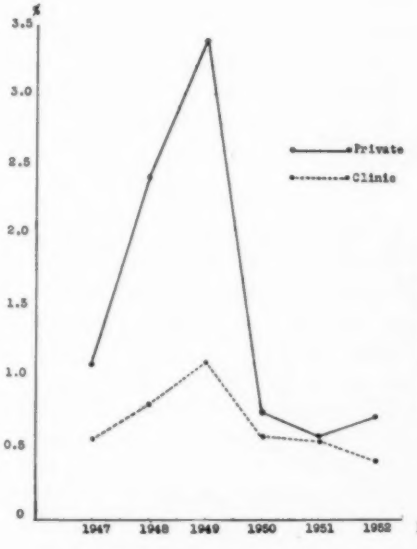


Fig. 3.—Influence of mother's status (private or clinic) on incidence of skin infections, 1947 to 1952.

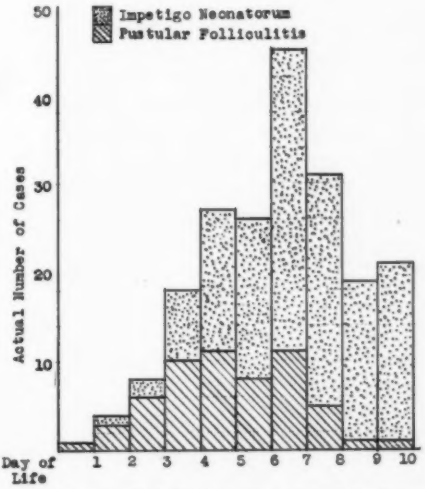


Fig. 4.—Relation of day of life to day of onset of skin infections over a six-year period, 1947 to 1952.

In our institution, as apparently in many others, skin infections occur more frequently in babies of private white mothers than in those of mothers on ward status whether white or Negro, as may be seen in Fig. 3. Racial skin differences might explain the low incidence in Negro infants, but the relation of incidence to the private or ward status of the white

for the first four to five days.[8] We, too, have noted the appearance of skin infections to be infrequent before the fourth day of life but to rise rapidly thereafter, the peak of incidence being on the seventh day. (See Fig. 4.) Opportunity for infection apparently increases with the length of time spent by the baby in a congregate nursery.

Another important factor might be the necessity of accommodating an ever-increasing number of mothers and babies without a proportional increase in either space or nursing staff. For example, in 1940, there were 1,880 live births in the St. Louis Maternity Hospital, and in 1952, 3,841 live-born infants.

The Standards and Recommendations for Newborn Care[9] as established by the American Academy of Pediatrics have always been a guide for our nursery policies. Because of the tremendous increase in babies served and the chronic shortage of personnel, these regulations could not always (and cannot now) be fulfilled in the following respects:

(1) Number of babies per nursery unit. We often have to accommodate as many as twenty-five babies in a nursery unit. Space in the unit is still adequate in respect of square footage, however.

(2) Number of babies per attendant or nurse. Although at least two individuals normally staff each nursery, it is not unusual to have only one girl on a given shift.

(3) Nasopharyngeal cultures on all nursery personnel. Also, although theoretically persons suffering from respiratory or other infections are excluded from nursery duty, one must be realistic in stating that because of a shortage of relief help we undoubtedly have had and will continue to have persons working in the prodromal stages of such infections or returning to duty when not yet bacteriologically acceptable.

Another more subtle factor may be the gradual change in the type of nursery personnel. Since World War II, it has never been possible for us, with five separate nurseries, to obtain enough registered nurses for three shifts in other than the Premature-Observation Unit, where skin infections have never been a problem. Thus the majority of our full-term babies are now cared for by nursing attendants. The implications of a considerable dependence on a nonprofessional, shifting personnel are obvious.

In view of these several factors, perhaps it is not too surprising that a standard routine of pHisoderm baths on alternate days has proved more satisfactory than the "inspection bath" which in our opinion leaves too much to individual initiative.

SUMMARY

1. The incidence of impetigo neonatorum in a large maternity hospital over a six-year period is reported.

2. Dry care was used for approximately the first half of the interval mentioned, 1947, 1948, and 1949. During these years the incidence of impetigo was 0.91 per cent, 1.32 per cent, and 2.00 per cent of 3,393, 3,203, and 3,189 live births, respectively.

3. During the second half of the six-year period mentioned, 1950, 1951, and 1952, the babies were bathed every other day with a spray technique, using a sudsing detergent especially suitable for newborn skin. The incidence of impetigo during these years was 0.29 per cent, 0.29 per cent, and 0.13 per cent of 3,356, 3,772, and 3,841 live births, respectively.

4. In our experience, babies of private white mothers have more skin infections than babies of clinic mothers whether white or Negro. The re-

lationship of the longer hospital stay of the first group is mentioned.

5. The gradual but inexorable increase in the nursery population over the last twelve years is mentioned. Thus double the number of babies must now be cared for without doubling either nursing staff or space facilities.

6. The possible relationship of an ever-increasing dependence on a shifting, nonprofessional personnel is suggested.

7. A combination of these factors is probably more significant than any one alone.

8. This experience suggests the desirability of individualizing institutional practices to conform with the situation as it presents.

REFERENCES

1. Sanford, H. N.: Care of the Skin of the Newborn Infant, J. PEDIAT. **11**: 68, 1937.
2. Parmelee, A. H.: Skin Conditions in the Newborn, M. Clin. North America **30**: 17, 1946.
3. Lee, H. F., Wilson, R. B., Brown, C. E., and Reed, J. P.: Impetigo and Acute Infectious Exfoliative Dermatitis of the Newborn Infant (Ritter's Disease), J. PEDIAT. **41**: 159, 1952.
4. Farquharson, C. D., Penny, S. F., Edwards, H. E., and Barr, E.: The Control of Staphylococcal Skin Infections in the Nursery, Canad. M. A. J. **67**: 247, 1952.
5. Allers, O. E., Hubbell, J. P., Jr., and Buck, A.: A Rapid Aseptic Scrub Technique for Nurseries of the Newborn, Am. J. Obst. & Gynec. **60**: 431, 1950.
6. Reid, D. E., Walter, C. W., and Buck, A.: Surgical Scrubbing With pHisoderm G-11 as Applied to a Maternity Hospital, Surg., Gynec. & Obst. **91**: 537, 1950.
7. Chilsholm, T. C., Duncan, T. L., Hufnagel, C. A., and Walter, C. W.: Disinfecting Action of pHisoderm Containing Three Per Cent Hexachlorophene on the Skin of the Hands, Surgery **28**: 812, 1950.
8. Osborne, E. D., Ross, J. R., and Wrong, N. M.: Pediatric Dermatology: Round Table Discussion, Pediatrics **10**: 710, 1952.
9. Standards and Recommendations for Hospital Care of Newborn Infants—Full-Term and Premature, Committee on Fetus and Newborn, American Academy of Pediatrics, 1948.

OSTEOGENESIS IMPERFECTA CONGENITA IN CONSECUTIVE SIBLINGS

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THE hereditary aspects of osteogenesis imperfecta congenita are usually not considered prominent, whereas in the infantile type and the late type the disease definitely follows a dominant mendelian trait. Blue sclerae, frequent fractures, and deafness are seen in that order of frequency in the afflicted families of the infantile and late types, as a definite hereditary factor which has been reported to follow through at least seven generations. The birth of two consecutive siblings with the congenital type, however, is not characteristic and is unexpected.

Because of the early death of most infants with the congenital type of osteogenesis imperfecta, heredity does not usually appear to play an important role. When fractures are present at birth, blue sclerae and otosclerosis do not appear to be prominent features. It is for these reasons that we feel these two cases of the congenital type in siblings should be reported.

These two cases of the congenital type of osteogenesis imperfecta occurred in consecutive siblings of the same parents, representing the second and third offspring. The firstborn child is apparently mentally and physically normal. The diagnosis was obvious at birth in each case and was substantiated by laboratory and x-ray findings. The blood chemistry findings were within normal limits in each case as usually is found in this condition. The x-ray findings of changes in the bone of the skull, the long bones, and in the bodies of the vertebrae in both cases are those usually seen in osteogenesis imperfecta. Both infants followed the same clinical course with death occurring after the onset of an intercurrent respiratory tract infection which failed to respond to antibiotics. The first sibling expired at 5½ months after gaining 4 pounds 4 ounces since birth. The second sibling expired at 5 months after gaining 1 pound 4 ounces. No specific therapy was administered in either of these cases.

From the Pediatric Service of Dr. Harry S. Altman, Lincoln Hospital.

CASE REPORTS

History of First Infant (S. R.).—A 2½-month-old female infant was born on Feb. 16, 1949, by normal spontaneous delivery. The prenatal course was uneventful, and the duration of labor was eight hours. The first child is living and well. At the time of delivery in another hospital the physician in attendance noted that the baby had many deformities of the bones of her extremities and ribs. Her birth weight was 5 pounds 13 ounces. Because it was thought by the family physican that the infant needed orthopedic care, she was brought to Lincoln Hospital. Prior to admission to Lincoln Hospital the infant developed many fractures of its bones as shown by the physical examination and by x-ray.

Physical examination on admission revealed an alert, well-nourished fe-

male infant in good nutritional state with good cry. The weight was 8 pounds. The principal physical findings were as follows: The head showed a flattening of the posterior aspect due possibly to position and palpation of the head gave the sensation of holding a bag of bones. Sclerae of both eyes were definitely blue. The ear, nose and throat were essentially normal. The heart was of normal size and had a regular sinus rhythm. No normal sounds were heard. The lungs were clear to percussion and auscultation. Examination of the abdomen revealed a linear edge palpable at one fingerbreadth below the right costal margin and a herniation in the region of the umbilicus. There were multiple healed fracture deformities of all extremities giving them a grotesque appearance. Motion was possible in the extremities at sites other than the anatomical joints, representing pseudojoints. Crepitance was evident at the sites of recent fractures.

The diagnostic impression was: osteogenesis imperfecta congenita, and umbilical hernia.

X-rays taken on admission were read as showing marked osteogenesis imperfecta of the entire skeleton with broadening of the bones. The cranial tables were very thin. Lateral views of the spine revealed a marked thinning of vertebral bodies and kyphosis at L_1.

Laboratory findings on admission: red blood count, 2,500,000 per cubic millimeter; hemoglobin, 50 per cent; white blood count, 12,300 per cubic millimeter with a differential count of segmentals 44 per cent, lymphocytes 50 per cent, monocytes 6 per cent.

Urinalysis was negative for albumin, sugar, and acetone. Microscopically uric acid crystals were present.

Blood chemistry: calcium (serum), 10.6 mg. per cent; inorganic phosphorus, 4.2 mg. per cent; alkaline phosphatase, 13.0 Bodansky units; albumin, 4.0 Gm. per cent; globulin, 2.0 Gm. per cent; total protein, 6.0 Gm. per cent.

Course in hospital: The infant developed a nasal discharge and a slight elevation in temperature which persisted in spite of antibiotics and symptomatic therapy. She showed a weight gain of one pound during hospitalization. She continued to develop fractures of the extremities in spite of efforts to prevent them. Therapy was mainly supportive. Approximately three months after admission the infant developed clinical signs of bronchopneumonia and although increased doses of antibiotics were given, she expired at approximately 5½ months of age.

Anatomical diagnosis at post mortem: bronchopneumonia; osteogenesis imperfecta; several, old, healed pathological fractures; umbilical hernia.

History of Second Infant (W. R.).—This 3-week-old female infant was born on Oct 20, 1952, by normal spontaneous delivery. At the time of delivery the parents were told that this infant had fractures of many of the bones of her body. The infant was brought to Lincoln Hospital for further study. The mother's prenatal course was uneventful.

Physical examination on admission revealed a 3-week-old female infant in no acute distress, who was small, with obvious deformities of the extremities. Weight on admission was 5 pounds 8 ounces.

On physical examination both cranium and face showed some asymmetry. There was flattening of the posterior aspect of the head to a marked degree. Both fontanels appeared to be full. Palpation of the head gave the sensation of a "bag of bones." The infant apparently could not move or turn her head from side to side.

There was a definite light blue tingeing of the sclerae of both eyes. Ears, nose, and throat were normal. Heart rate, rhythm, and sounds were essentially normal. The lungs were clear to auscultation and percussion. An angular deformity was present on the right side of the thoracic cage in

the nipple line over the fifth and sixth ribs. A small herniation existed at the site of the umbilicus in the anterior abdominal wall. Very little if any active motion of the extremities was noted. There was lateral bowing of the upper portion of the left arm, pain being elicited by palpation at this site. The right upper extremity appeared shortened but not deformed. It was apparently painful to palpation. Several areas of tumefaction were present over both lower extremities. Both legs and thighs showed anterior bowing and extension of the knee completely was impossible.

Fig. 1.

The impression on admission was osteogenesis imperfecta, multiple fractures, and umbilical hernia.

The x-ray on admission (Fig. 1) showed marked osteogenesis imperfecta of the extremities with multiple recent and healed fractures. The cranial tables appeared extremely thin. The bodies of the vertebrae showed marked thinning and there was slight kyphosis at the junction of the thoracic and lumbar spine.

Laboratory findings on admission: red blood count, 3,800,000 per cubic millimeter; hemoglobin, 14 grams; differential—segmentals 46 per cent, stabs 6 per cent, lymphocytes 48 per cent.

Urinalysis was negative for albumin, sugar, and acetone. Microscopically uric acid crystals were present.

Blood chemistry: Calcium, 10 mg. per cent; alkaline phosphatase, 12 Bodansky units; phosphorus, 4.6 mg. per cent; total protein, 6.8 Gm. per cent; albumin, 3.9 Gm. per cent; globulin, 2.9 Gm. per cent.

Course: The infant was placed on an evaporated milk formula and supplemental vitamin therapy. She showed very little gain in weight although she took the feedings well. The infant died unexpectedly at approximately 20 weeks of age. No change in the initial x-ray findings was noted on subsequent films.

Anatomical diagnosis: osteogenesis imperfecta; bronchopneumonia; old healed fractures of all long extremities; umbilical hernia.

DISCUSSION

Osteogenesis imperfecta is a disease of osseous tissue manifested by extreme fragility of bones and often associated with blue sclerae. Fractures may occur during or immediately after birth, at the time the infant begins to walk, or later in childhood. Accordingly, the disease has been divided into three clinical types: the congenital, occurring at birth; the infantilis type, occurring at the time the infant attempts to walk, and the late type, occurring later in childhood. The discussion will be confined to the congenital type since it is applicable to the cases presented.

The principal gross pathological feature is the brittleness and deformities of the bones. Although all of the osseous tissue of the body is apparently affected, the changes in the long bones are most striking. The long bones show varying degrees of deformity depending upon the number and frequency of fractures. The relation between the metaphysis and epiphysis appears normal but the diaphyseal portion of bone is usually enlarged. Pseudojoints may develop at sites in the bones where fractures are frequent and healing has not been complete.

In the congenital type the fractures occur either in utero or during delivery, and involve the ribs, clavicle, and the bones of upper and lower extremities. The skull gives a very peculiar sensation on palpation and may be likened to holding a bag of water or a sack of stones. There are no consistent gross abnormalities of the other systems of the body. Microscopically, the deficiency of osteoblasts is striking. The cortex of the bone shows marked thinning and there is a scarcity of matrix. The trabeculae of the new bone are fragile. The periosteum is usually quite thin. The lamellar type of bone formation is absent. It has been noted in the callus which forms that the spacing of the osteoblasts is more regular and the development proceeds further. The sclerae appear to be about one-third the usual thickness.

It has been shown that the total ash of the bones of these patients is diminished and that the osteoporosis which is seen is due to calcium deficiency. The greater progress of bone development as seen in callus forma-

tion as compared to the original bone may be correlated with the higher phosphatase activity of callus. The blood calcium, phosphorus, and alkaline phosphatase values are within normal limits. The retention of calcium and phosphorus in osteogenesis imperfecta is about one-half to one-third that seen in normal subjects.

The exact mechanism for the development of osteogenesis imperfecta is not clear; however, Weber postulates that osseous tissue in osteogenesis imperfecta represents pathologic fiber bone. Representing the first stage of bone development after emergence from the endothelial cells of the blood vessels, fiber bone is the oldest type of bone. In osteogenesis imperfecta there is a lack of lamellar bone formation which is the highest stage of bone development. The lack of lamellar bone formation and the presence of pathological fiber bone may represent the defect in mesenchymal tissue which is postulated as the fundamental pathology of this condition.

The congenital type of osteogenesis imperfecta usually does not exhibit a familial tendency. The incidence is slightly higher in males. The most striking clinical feature is a softness of the cranial vault which gives a sensation upon palpation of grasping a "bag of bones." During the ensuing months of life the head subsequently shows deformities in the occipital and temporal regions. Due to multiple fractures at the time of birth, the trunk and extremities show grotesque deformities. Crepitance to palpation and pseudojoints are evident. Blue coloration of the sclerae is usually seen. These patients rarely survive infancy, and usually fall prey to some intercurrent infection.

Osteoporosis characterized the x-ray findings in this condition. The characteristic features are marked thinning of the cortex, diminution of the thickness of the shaft of the bone with some flaring toward the diaphysis, normal epiphyseal-metaphyseal relationship, and coarseness of the trabeculation. An outstanding feature during the early days of life is the presence of various stages of callus formation about the multiple fractures. The ribs usually show more callus than the long bones. The skull shows multiple areas of ossification giving a mosaic pattern. Ossification centers are normal. The vertebrae may show some compression.

Therapy has generally been unsatisfactory in this condition. Some enthusiasm has been acclaimed for estrogenic and androgenic therapy. In view of the futility of all other methods, these may be employed for what they are worth. The principal therapy involves careful handling of the infant to prevent further fractures and maintenence of the nutritional state, as well as the treatment of intercurrent infections.

SUMMARY

Two consecutive siblings born with congenital osteogenesis imperfecta are described and discussed.

BIBLIOGRAPHY

Brennemann's Practice of Pediatrics, vol. IV, chap. 23, p. 33.

Orlandini, I. Early Congenital Osteogenesis Imperfecta, Ann. radiol. diag. **22**: 186, 1950.

Ottley, C. M.: Osteopsathyrosis (Lobstein's Disease); A Critical Review, Arch. Dis. Childhood **7**: 137, 1932.

Ottley, C. M.: Lobstein's Syndrone, Arch. Dis. Childhood **27**: 131, 1952.

Wright, P. B., Gernstetter, S., and Greenblatt, R. B.: Therapeutic Acceleration of Bone Age in Osteogenesis Imperfecta, J. Bone & Joint Surg. **33-A**: 939, 1951.

ATRIAL SEPTAL DEFECT IN INFANTS AND CHILDREN

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CARDIAC surgery has recently been extended to include the repair of defects of the atrial septum. Successful closure of such defects in living patients has been reported by Murray,[1] Swan,[2] Gross,[3] Bailey and associates,[4] and Lewis and Tauffic.[5] The development of these new operations has further emphasized the importance of early and accurate diagnosis of congenital cardiac anomalies. It has become even more important to differentiate those cases in which an atrial septal defect is the major abnormality from those in which this is only one of a combination of defects. In the latter instance, the presence of the atrial defect may frequently be obligatory for survival. In addition, it has now become necessary to establish the indications for surgery on patients with primary atrial septal defects.

The clinical and pathological features of this disease have been reviewed by Roesler,[6] Bedford and coworkers,[7] and Taussig and associates.[8, 9] The introduction of cardiac catheterization has permitted more accurate and earlier diagnosis during life. The youngest reported series in which the diagnosis was confirmed by physiological studies is that of Keith and Forsyth.[10] The ages in their group ranged from 22 months to 13 years, with an average of 7.7 years.

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It is the purpose of this report to emphasize that uncomplicated atrial septal defects may be the cause of serious difficulty and death in infancy, and that since surgery may salvage some of these infants, greater effort should be directed toward the problem of early accurate diagnosis. Our experience during the past four years with infants and children diagnosed as atrial septal defect by heart catheterization or autopsy will be presented. We also wish to point out some of the difficulties which may be encountered in the use of heart catheterization.

MATERIALS AND METHODS

The post-mortem material of the Department of Pathology, University of Minnesota, during the years 1949 to 1952 was reviewed. In infants under one year, six cases were found in which the underlying cause of death was considered to be an uncomplicated atrial septal defect. Complete clinical studies were not available on the majority of these patients, however.

The twenty-one patients chosen for the major portion of this study include all those seen in the Pediatric Cardiac Clinic at the University of Minnesota Hospitals in which a diagnosis of atrial septal defect was made by cardiac catheterization. Four were infants while the other seventeen were between 2 and 16 years of age. All patients were evaluated by

clinical history, physical examination, electrocardiography, x-rays, and fluoroscopy. Heart catheterization was performed in a manner previously described.[11] Oxygen content of blood samples was determined by the method of Van Slyke and Neill.[12] Pressures were recorded using a strain gauge, and the tracings made in part by direct-writing apparatus and in part by photographic methods. Mean pulmonary artery pressures were obtained by planimetry.

A rise in oxygen content of over 1.9 vol. per cent[13] between the blood in the superior vena cava and the right atrium was accepted as indicating the presence of a shunt into the right atrium. In three cases an inferior vena cava sample was used. Values between 2 and 2.8 vol. per cent were considered significant in these three cases in view of the presence of supportive findings such as the passage of the catheter through the defect, demonstration of the defect by angiocardiography, or postmortem examination. An increase of over 0.9 vol. per cent[13] in the right ventricle over the right atrium was considered evidence of a ventricular septal defect.

Nine cases previously classified as atrial septal defect following catheterization were excluded because they did not fulfill our criteria. Two cases showed evidence of a ventricular septal defect in addition to the atrial defect. In an additional two cases, no atrial shunt was demonstrated, but the catheter was noted to enter the left atrium and pulmonary vein. We interpreted this as the passage of the catheter through a patent foramen ovale. The latter two cases did, however, show evidence of shunt into the right ventricle thereby accounting for the clinical and roentgen findings. The suggestion of mitral atresia and common atrium was so strong in another case that this was excluded. In two instances, catheterization data were suggestive but the patients expired at home and no autopsy could be done. Incomplete anomalous pulmonary venous return was suggested in a further case, while in another the clinical picture indicated a different diagnosis.

OBSERVATIONS

Infant Deaths.—Review of our postmortem material of 202 cases of congenital heart disease in children revealed eleven cases of uncomplicated atrial septal defect. An anatomically patent foramen ovale with a flap was not considered a defect. In two instances death resulted from attempts at corrective surgery. Problems not directly related to the heart were possible causes of death in three. Thus six cases of infants all under one year of age remain where the cardiac defect was considered the underlying cause of death. These are reviewed in Table I. Only two were observed clinically in this institution.

Death occurred between the ages of 59 hours and 7 months. Five expired because of cardiac decompensation, while the other one succumbed to pneumonia presumably precipitated or aggravated by the heart malformation. Two patients (B. T. and M. J. P.) were known to have congential heart disease at birth. Several episodes of paroxysmal tachycardia were observed in one (J. K.).

The history of B. T., born at University Hospitals, is of interest. Pregnancy and delivery were normal,

TABLE I. SUMMARY OF FINDINGS IN INFANTS UNDER ONE YEAR WITH ATRIAL SEPTAL DEFECT DIAGNOSED AT AUTOPSY

NO.	NAME AND SEX	AGE AT DEATH	CLINICAL FEATURES								ROENTGEN*		POST MORTEM
			FEEDING PROBLEM	RESPIRATORY DISEASE	SLOW GROWTH	DYSPNEA	CARDIAC FAILURE	EPISODES OF CYANOSIS	MURMUR	THRILL	CARDIAC ENLARGEMENT	INCREASED PULMONARY VASCULATURE	
1.	B. T. ♂	59 hr.	0	0	0	+	+	+	Systolic	+	Marked	Moderate	A.S.D. - 2 cm.
2.	C. P. ♀	2 mo.	+	-	+	+	+	+	Systolic	0	-	-	A.S.D. - 8 mm.
3.	M. J. P. ♀	2 mo.	+	+	+	+	-	-	Systolic	-	Moderate	Moderate	A.S.D. - 1 cm.
4.	P. W. ♀	5 mo.	-	+	-	+	+	+	-	-	Moderate	Moderate	A.S.D. + P.F.O.
5.	R. C. ♂	6 mo.	+	0	+	+	+	+	-	-	Moderate	Moderate	A.S.D. - 2 cm.
6.	J. K. ♀	7 mo.	+	+	-	+	+	-	Systolic	-	Moderate	Moderate	A.S.D. - 2 cm.

+ — Positive history.
0 — Negative history.
- — Information not available.

*Anteroposterior films only.
A.S.D. — Atrial septal defect.
P.F.O. — Patent foramen ovale.

TABLE II. CLINICAL, ELECTROCARDIOGRAPHIC, AND ROENTGEN FINDINGS IN CATHETERIZED PATIENTS WITH ATRIAL SEPTAL DEFECT

CASE	AGE IN YEARS	SYMPTOMS	GROWTH RETARDATION	CARDIAC FINDINGS	ECG	ROENTGEN					COMMENTS
						SIZE	R.V.	P.A.	PULM. VASC.	AORTA	
B. D. ♀	½	Feeding problem; repeated pneumonia; excessive perspiration; ? cardiac failure	+	Systolic murmur, LSB and apex	L.A.D. R.V.H. Peaked P_2	+++	+++	++++	+++	-1	Murmur first heard at 6 wk. A.S.D. demonstrated by angiocardiogram
B. J. ♀	1⅓	Feeding problem; dyspnea; repeated pneumonia; episodes of cyanosis	+	Systolic murmur, 2nd RIS; ? diastolic component; loud P_2	R.A.D. R.V.H.	++	++	?	++	?	Murmur heard at birth. Dextrocardia
S. J. ♀	1⅓	Feeding problem; dyspnea; repeated pneumonia; episodes of cyanosis; cardiac failure	+	Systolic murmur, pulmonic area; loud P_2	No A.D. No V.H.* Peaked P_2	++	++	++++	++	-1	Murmur heard at birth. Died during attempt to repair defect. Autopsy—A.S.D. in lower atrial septum
V. R. ♀	1½	Feeding problem; dyspnea; excessive perspiration	+	Precordial bulge; systolic murmur; 3rd, 4th, and 5th LIS; P_2 loud; faint diastolic murmur along LSB	L.A.D. R.V.H.	++	++	++++	++	-1	Murmur heard at birth.
D. L. ♀	4½	Asymptomatic	0	Systolic murmur, 3rd and 4th LIS	No A.D. Suggestive R.V.H.	N	+	++	+	-1	Murmur first heard at 4 yr.
P. A. ♀	5	Dyspnea; decreased exercise tolerance; repeated pneumonia; cardiac failure; episodes of cyanosis with exertion	+	Precordial bulge; thrill, apex and LSB; systolic murmur, 1st and 2nd LIS; diastolic murmur, 3rd and 4th LIS; P_2 loud	R.A.D. R.V.H. Big P_1 & P_2 Prolonged P-R	+++	++	+++	+++	-1	Died following attempt at surgical repair. Autopsy—semicircular defect in lower atrial septum. Difficulties started in infancy
J. M. ♂	5	Frequent respiratory infections; slow development	0	Thrill, LSB; precordial bulge; systolic murmur, 1st and 2nd LIS; diastolic murmur, apex	L.A.D. R.V.H. Big P_2 Prolonged P-R	++	++	++	++	N	Murmur first heard at 8 mo.
G. B. ♀	5	Asymptomatic	0	Systolic murmur, 2nd and 3rd LIS	R.A.D. R.V.H. Prolonged QRS	++	+	+	U.L.N.	-1	Murmur first heard at 5 yr.

J. J. ♀	5	Frequent respiratory infections; irritability	+	Precordial bulge; systolic murmur, 2nd and 3rd LIS; P_2 loud	R.A.D. R.V.H.	++	++	+ +++	N	Murmur first heard at 4 yr. Successful repair of defect
S. S. ♀	5	Dyspnea; decreased exercise tolerance, considerable	+	Precordial bulge; thrill, 1st and 2nd LIS; systolic murmur, 3rd LIS; diastolic murmur, 3rd and 4th LIS; P_2 loud	No A.D. No V.H. Big P_2	+++	+++	++ ++	-1	Murmur first heard at birth
J. H. ♂	9	Frequent respiratory infections and pneumonia	+	Systolic murmur, 3rd LIS; ? diastolic component, 4th LIS; P_2 loud	No A.D. R.V.H.	+	N	+ +	-1	Murmur heard at birth
S. D. ♀	9	Asymptomatic	0	Systolic murmur, 2nd LIS; P_2 loud	R.A.D. No V.H.* Prolonged P-R	+	+	++ ++	N	Suspect rheumatic fever but diagnosis never definite.
R. G. ♂	9	Dyspnea; marked decrease exercise tolerance; frequent respiratory infections; cardiac failure several times	+	Precordial bulge; systolic murmur, 2nd LIS; P_2 loud	R.A.D. R.V.H. Rt. B.B.B.	++	++	+ +++	N	First episode cardiac failure at age 4 yr. Feeding problem in infancy. Murmur heard at 4 yr. Successful closure of defect
J. J. ♂	12	Asymptomatic	+	Slight precordial bulge; systolic murmur, 2nd LIS; diastolic murmur, 5th LIS; P_2 loud	L.A.D. No V.H. Big P_2 & P_3 Prolonged P-R	N	N	++ ++	N	No known abnormality until routine chest x-ray. Murmur heard at 12 yr.
B. B. ♀	12	Asymptomatic	0	Thrill, LSB; systolic murmur, 4th LIS	No A.D. No V.H.	N	N	++ ++	-1	Murmur heard on routine physical
D. W. ♂	12	Dyspnea; marked decrease exercise tolerance	+	Thrill, apex; systolic murmur, apex; diastolic murmur, apex, after exercise; P_2 loud	R.A.D. R.V.H. Rt. B.B.B. Extrasystoles	+++	+++	+++ ++	-1	Frequent respiratory infections and pneumonia in infancy. Murmur first heard at 3 yr.
T. P. ♂	13	Asymptomatic	+	Slight precordial bulge; thrill, 3rd LIS; systolic murmur, 2nd LIS; ? diastolic component, 4th and 5th LIS	R.A.D. R.V.H. Peaked P_1 & P_2 Prolonged P-R Rt. B.B.B.	N	+	++ ++	N	Murmur heard on routine physical.

TABLE II.—CONT'D

CASE	AGE IN YEARS	SYMPTOMS	GROWTH RETARDATION	CARDIAC FINDINGS	EGG	ROENTGEN SIZE	R.V.	P.A.	PULM. VASC.	AORTA	COMMENTS
R. L. ♂	12	Dyspnea; moderate decrease in exercise tolerance; repeated respiratory infections	0	Systolic murmur, 2nd and 3rd LIS.	R.A.D. No V.H.	N	+	++	+	N	Murmur heard first at age 9 yr. Successful closure of defect
G. K. ♂	13	Asymptomatic	0	Systolic murmur, 2nd and 3rd LIS	No A.D. No V.H.*	N	+	+	+	-1	Murmur heard on routine physical age 13 yr.
K. H. ♀	14	Asymptomatic	0	Systolic murmur, 3rd LIS; P_2 loud	R.A.D. R.V.H. Big P_2	++	N	+	++	-1	Murmur heard in first few years.
J. V. H. ♂	16	Dyspnea; decrease in exercise tolerance, slight; ↑ episode failure age 13.	+	Systolic murmur, base; diastolic murmur, apex; P_2 loud	No A.D. No V.H.* Prolonged P-R Rt. B.B.B.	N	+	++	+	-1	Murmur heard first in childhood.

LSB – Left sternal border.
RIS – Right interspace.
LIS – Left interspace.
R.A.D. – Right axis deviation.
L.A.D. – Left axis deviation.
R.V.H. – Right ventricular hypertrophy.
*Standard leads only.
+Growth retardation present.

+ — Mild.
++ — Moderate.
+++ — Severe.
-1 — Hypoplastic.
N — Normal.
U.L.N. — Upper limits of normal.
B.B.B. — Bundle branch block.

but at birth he was noted to have a loud systolic murmur and thrill along the left sternal border. Otherwise he appeared normal and the first day of life was uneventful. Roentgenograms showed a markedly enlarged heart with increased pulmonary vasculature, and the electrocardiogram showed right axis deviation and right ventricular preponderance consistent with age. He was seen by one of us and a clinical diagnosis of atrial or ventricular septal defect was made. On the second day, cyanosis, dyspnea, and cardiac failure were noted. Despite oxygen and digitalis therapy his condition deteriorated and he expired 59 hours after birth. Autopsy showed an atrial septal defect 2 cm. in diameter with a fibrous strand dividing it in half.

Patients Studied With Cardiac Catheterization.—

Clinical Features: A summary of the clinical, electrocardiographic, and roentgen findings of the twenty-one patients who were catheterized is listed in Table II.

All of the infants studied had symptoms which could be attributed to their cardiac disease. Feeding difficulties, recurrent upper respiratory infections and pneumonia, and growth retardation were the commonest complaints. In several cases, the parents stated that the infant perspired excessively and had rapid respirations. Of the group of seventeen over 2 years of age, only nine had symptoms, and in three cases these dated back to infancy. A history of repeated respiratory tract infections was obtained in six. Six complained of dyspnea on exertion and decreased exercise tolerance.

All of the infants showed evidence of growth retardation when plotted on the Wetzel Grid. However, only nine of the seventeen older children were of less than average physique and showed a rate of growth below the 67 per cent auxodrome. The others were of average physique and growing at a normal rate, but none were stocky.

Persistent cyanosis was not observed in any patient. Transient episodes of cyanosis were reported in two infants, each time associated with decompensation and/or pneumonia. Mild cyanosis with exertion occurred occasionally in one of the older children who was in latent failure much of the time. Definite cardiac failure was observed in at least one infant and two children. The first episode of failure in the children occurred between the second and fourth years of life. In several other instances we were unable to ascertain definitely whether or not the patient was in failure.

Suspicion of the possibility of congenital heart disease was first aroused in most cases by the detection of a heart murmur on routine physical examination by the family physician. The murmur was heard at birth in five cases, during the first year in two, and subsequently in fourteen. Heart failure, pneumonia, enlarged heart on routine chest x-ray, and a suggestive history of rheumatic fever were responsible for bringing the patient to a physician in the other cases. None of the patients had definite rheumatic fever.

Cardiac Findings: A precordial bulge was noted in one infant and seven children. Many had an increased precordial thrust with displacement to the left of the apex beat, and cardiac enlargement to percussion was frequently noted. A systolic thrill was present in six children but in no

infants. Usually these thrills were felt along the left sternal border, most often in the first, second, and third interspaces. In one case proved at post mortem the thrill was felt best at the apex.

The auscultatory findings were variable, though a systolic murmur of moderate intensity was heard in every patient. Usually the murmur could be heard over much of the precordium but best along the left sternal border. In the children the murmur was quite consistently loudest in the first three interspaces but in the infants the point of maximum intensity was anywhere along the left sternal border or at the apex. Diastolic murmurs were heard definitely in seven cases, four along the left sternal border and three at the apex. The apical diastolic murmurs did not resemble those heard in mitral stenosis. There appeared to be some relationship between the loudness of the systolic murmur, presence of a thrill, and presence of a diastolic murmur, to the heart size. The second pulmonic sound was accentuated in over half the cases, suggesting increased pressure in the pulmonary circuit. This was usually best heard in the third left intercostal space when the murmur was of maximum intensity in the pulmonic area.

Taussig[9] states that the blood pressure is low and the pulse pressure narrow in these patients. However, only one in our series had a blood pressure lower than normal and in no instances was an abnormal pulse pressure found.

Electrocardiographic Findings: In seventeen cases, unipolar lead tracings were taken in addition to those of the standard leads. Tracings were normal in two patients, border line in three, and abnormal in sixteen. Right axis deviation was present in ten cases. Left axis deviation was found in four and was interpreted as being due to rotation and cardiac position. Right ventricular hypertrophy was present in twelve tracings. In several instances where the standard leads showed normal or left axis deviation, right hypertrophy was demonstrated in the unipolar leads. Kroop and associates[14] have indicated that rotation and position of the heart are more important than chamber hypertrophy alone in determining extremity potentials and, therefore, axis deviation. Less than half of our patients had peaked P waves in one or more leads. There was prolongation of the P-R interval in six, and complete or incomplete right bundle branch block in four. No significant abnormalities of rhythm were observed.

Roentgen Findings: Cardiac enlargement was observed in the posteroanterior view in fourteen cases. However, seventeen had definite right ventricular enlargement, noted particularly in the left oblique position. In some of the larger hearts the left side became abnormally prominent in the left anterior oblique view because of displacement of the left ventricle by the enlarged right ventricle. In no patient was enlargement of the left atrium noted. In general, there was no relationship between the heart size and the clinical condition of the older patients. Some older children with grossly enlarged hearts were leading active and normal lives. However, all the infants had greatly enlarged hearts and were symptomatic. The pulmonary artery was prominent in every case, and the hilar and peripheral

pulmonary vascular markings increased in all but one. In this patient the markings were considered to be at the upper limits of normal.

rior position in three infants were remarkably similar. We did not observe expansile hilar pulsations as frequently as others have reported.

A.

B.

C.

Fig. 1.—S. J., 15 months of age. *A*, Posteroanterior position. *B*, Left anterior oblique position. *C*, Right anterior oblique position.

Pulmonary artery dilatation was unusually marked in the infant group. Roentgenograms in the posteroante-

The aorta appeared definitely hypoplastic in more than half of the patients.

Figs. 1, 2, and 3 represent roentgenograms of three cases of atrial septal defect in infants. The similarity of the cardiac silhouette in the posteroanterior projection and the prominent pulmonary artery segment are notable.

Cardiac Catheterization: The data obtained by cardiac catheterization are summarized in Table III.

In all but five cases the catheter was introduced through the median basilic vein, usually of the left arm. In four infants and one 5-year-old

Fig. 2.—V. R., 18 months of age. Posteroanterior position.

Fig. 3.—B. D., 8 months of age. Posteroanterior position.
The similarity of the cardiac silhouette in the posteroanterior projection in Figs. 1, 2, and 3 is notable.

TABLE III. CATHETERIZATION RESULTS IN PATIENTS WITH ATRIAL SEPTAL DEFECT

CASE	O_2 CONTENT—VOLUMES PER CENT					O_2 SATURATION		PRESSURE—MM. HG			THROUGH DEFECT
	S.V.C.	I.V.C.	R.A.	R.V.	P.A.	F.A.	OTHER	R.V.	P.A.	MEAN P.A.	
B. D. (1)		9.0	10.8	- -	- -	90%	L.A. 95%	--	--	--	+
(2)		8.7	10.9	- -	- -	--	--	--	--	--	+
B. J.	8.3	6.9	10.4	10.2	10.4	90%	P.V. 100%	50/5	40/34	36	+
S. J.		6.1	8.9	9.6	9.7	--	P.V. 88%	50/10	50/30	44	+
V. R.	6.9	9.4	14.4	13.5	13.6	--	P.V. 94%	30/0	26/10	21	+
D. L.	9.9	- -	12.4	12.9	13.0	96%	--	24/2	16/12	13	0
J. M.	12.0	- -	15.2	15.0	15.0	100%	L.A. 96%	33/4	24/8	15	+
G. B.	8.7	- -	11.6	11.8	12.0	--	L.A. 100%	28/-10	26/6	17	+
J. J.	12.9	- -	14.9	15.1	15.1	100%	--	20/2	12/8	9	0
S. S.	- -	11.8	13.9	14.1	13.5	--	P.V. 99%	26/-10	20/0	8	+
P. A.	10.4	- -	13.6	13.3	- -	--	--	40/0	--	--	0
J. H.	10.8	- -	14.7	15.1	15.1	93%	L.A. 95%	18/0	14/4	10	+
S. D.	10.9	- -	13.8	14.0	13.6	100%	--	20/0	16/6	11	0
R. G.	13.6	- -	16.0	16.4	- -	96%	--	43/-3	--	--	0
J. J.	14.2	- -	16.1	16.8	16.7	--	L.A. 95%	10/-4	10/5	6	+
R. L.	10.7	- -	15.1	15.3	15.5	100%	--	30/0	18/6	12	0
B. B.	8.9	- -	13.8	14.2	14.6	99%	--	28/8	20/12	15	0
D. W.	8.9	- -	13.5	13.3	13.0	98%	--	28/0	24/6	12	0
T. P.	12.7	- -	15.3	15.7	15.5	--	L.A. 98%	25/-5	12/3	8	+
J. K.	10.6	- -	12.8	12.6	11.7	100%	--	20/4	18/12	14	0
K. H. (1)	11.7	- -	14.5	11.4	13.1	94%	P.V. 83%	36/-5	25/12	20	+
(2)	14.6	- -	17.9	17.2	17.5	--	P.V. 94%	26/-8	23/5	13	+
J. H.	12.0	- -	16.8	16.1	16.1	100%	--	27/0	20/8	13	0

child it was necessary to use the superficial femoral vein. Our experience has been that an arm vein can rarely be used in a patient under 2 years of age. When a leg vein was used, we were not always able to obtain a blood sample from the superior vena cava. Samples were obtained in the right ventricle and pulmonary artery in every case but three. In two we were unable to enter the pulmonary artery; in the third we failed to enter the right ventricle. In the latter instance we thought the presence of a ventricular septal defect was unlikely in view of our angiocardiographic findings.

When the catheter was passed through the defect a sample was obtained in the left atrium and/or pulmonary vein. Oxygen saturation was over 94 per cent in these samples in all cases but one. Femoral artery oxygen saturation was obtained in fourteen cases and the values ranged from 90 to 100 per cent. The catheter passed through the defect in eleven cases (approximately 50 per cent). It was much easier to get into the left heart when the inferior route was used, but it was more difficult to enter the right ventricle and pulmonary artery. Passage of the catheter into the left atrium was not considered evidence of a defect unless a shunt was demonstrated.

A mean pulmonary artery pressure of over 20 mm. of mercury was considered as definite evidence of pulmonary hypertension. Three patients had significantly elevated mean pulmonary artery pressures, the highest being 44 mm. In two others where the pulmonary artery was not entered we considered pulmonary hypertension to be present since the right ventricular pressures were elevated and there was no reason to suspect pulmonary stenosis. One of these cases (P. A.) was proved at post mortem not to have pulmonary stenosis, while the other (R. G.) showed no evidence of pulmonary stenosis at surgery. In no case was the pulmonary hypertension of a severe nature.

Slight differences in pressure between the pulmonary artery and right ventricle were observed in a number of cases. The right venrticular pressure was not elevated in any of these. Negative ventricular diastolic pressures were occasionally obtained. We believe that these findings were inherent in the method and apparatus used, mostly due to catheter whip. A mild relative pulmonary stenosis produced by the left-to-right shunt may have been another possible cause.

In three cases excluded from the general series, the right ventricular pressure was mildly elevated and the pulmonary artery pressure significantly lower. We considered these as examples of mild pulmonary valvular stenosis in addition to an atrial septal defect with left to right shunt. The findings in these cases are reviewed in Table IV. All three patients were symptomatic. The systolic murmurs were not different from those heard in the children mentioned earlier. In two, a thrill was present in the pulmonic area. The second pulmonic sound was loud in one, and not decreased in the other. The electrocardiograms showed right axis deviation and right ventricular hypertrophy. Cardiac enlargement was found on the roentgenograms. The pulmonary vascular markings were at the upper limits of normal in two

TABLE IV. CLINICAL, ELECTROCARDIOGRAPHIC, ROENTGEN, AND CATHETERIZATION FINDINGS IN PATIENTS WITH ATRIAL SEPTAL DEFECT AND MILD PULMONARY STENOSIS

CASE	AGE IN YEARS	SYMPTOMS	GROWTH RETARDATION	CARDIAC FINDINGS	ECG	ROENTGEN					COMMENTS
						SIZE	R.V.	P.A.	PULM. VASC.	AORTA	
A. K.	2½	Several episodes of pneumonia and cardiac failure after attack of spinal polio	+	Thrill, base; systolic, murmur, 3rd LIS; P_2 loud	R.A.D. R.V.H. Big P_1 & P_2	++	+++	++	++	-1	Murmur first heard at birth.
R. K.	8	Slightly decreased exercise tolerance	0	Thrill, 1st, 2nd, and 3rd LIS; systolic murmur, 2nd LIS	R.A.D. R.V.H.	+	+	++	U.L.N.	-1	Murmur heard first at age 6 mo.
M. W.	13	Dyspnea; decreased exercise tolerance	0	Systolic murmur, 2nd, 3rd, and 4th LIS	R.A.D. R.V.H. Rt. B.B.B.	+	+	+++	U.L.N.	-1	Murmur first heard ta age 13 mo.

CASE	O_2 CONTENT—VOLUMES PER CENT					O_2 SATURATION		PRESSURE—MM. HG.			THROUGH DEFECT
	S.V.C.	I.V.C.	R.A.	R.V.	P.A.	F.A.	OTHER	R.V.	P.A.	MEAN P.A.	
A. K.	11.8	--	15.5	15.3	15.4	93%	--	42/1	19/9	17	0
R. K.	12.2	--	15.4	16.1	16.0	97%	P.V. 96%	40/2	16/6	11	+
M. W.	14.9	--	16.8	--	17.0	--	L.A. 97%	40/-10	28/14	17	+

but in the third were definitely increased. Clinically, the diagnosis of isolated pulmonary stenosis was considered in R. K. but not in the others. In retrospect, because of the roentgen findings we should have considered the possibility of pulmonary stenosis clinically in M. W. The disproportion between the pulmonary artery dilatation and the vascular markings in these two cases was suggestive of pulmonary stenosis. These three cases are mentioned because we believe that their symptoms are due primarily to the atrial septal defect.

DISCUSSION

The presence of an atrial septal defect is rarely compatible with a full span of life. Roesler[6] found the average length of life was 36 years in those who died from this defect; Cosby and Griffith's[15] average was 49 years. From a review of our clinical and post-mortem material it is apparent that an uncomplicated atrial septal defect may sometimes cause more difficulty in infancy than in later childhood.

In our series of 202 autopsies on children with congential heart disease, we found the atrial septal defect to be the sixth commonest abnormality. This does not imply that the septal defect was the cause of death in each case, for in some it was considered that death may have been due to other factors. In Keith and Forsyth's[10] experience this defect was the thirteenth in autopsy frequency. Commoner types in order of frequency in our series were transposition of the great vessels, tetralogy, ventricular septal defect, aortic-mitral atresia, and coaretation of the aorta. All but two of our autopsied cases with atrial septal defect died during the first year of life, the youngest being 59 hours old. From the literature one cannot ascertain how often death occurs in infancy. The youngest patient in Abbott's[16] series was 3 months of age, but she did not indicate how many of her group died early in life. The actual incidence of this malformation is not known although various estimates have been made.

The manifestation of symptoms is subject to wide variation. An infant with a relatively large defect may die shortly after birth in cardiac failure. Because the right auricular pressure may be greater than that in the left auricle at birth and in early infancy, episodes of cyanosis may occur but this is not permanent.[9] Cyanosis later in infancy and childhood generally implies cardiac failure. Those who survive the immediate neonatal period may present with feeding problems, poor weight gain, or repeated attacks of pneumonia. Some require hospitalization for a significant portion of infancy. The mother often notes rapid, noisy respirations and profuse sweating. Cardiac failure may occur early. Since pulmonary edema and pneumonia give very similar signs in early life, the incidence of cardiac decompensation may be higher than we encountered. It is worth while noting that these symptoms are no different from those presented by patients with patent ductus arteriosus, aortic septal defect, and ventricular septal defect who are symptomatic in infancy. In general, those babies who survive the difficulty in infancy improve and do well for several years. Recurrent respiratory infections are, however, frequent. When school age is reached and general activity increases, the

most frequent complaints are a progressive decrease in exercise tolerance and dyspnea on exertion. Cardiac failure may occur.

There are those who have a benign infancy but develop symptoms at school age and are then unable to keep up with their playmates. In many of these a history of repeated respiratory infections in the past can be obtained. A significant number are asymptomatic and the possibility of congenital heart disease is not entertained until the family physician hears a murmur on routine examination, or cardiac enlargement is found during a chest survey. In general, children with atrial septal defects are able to engage in normal physical activity and lead normal lives.

We have noted the same preponderance of females to males as has been reported by other observers,[6, 10] the ratio being almost two to one in our series. The poor physical development and the gracile habitus of children with this disease have been emphasized in the past.[9] We tend to agree with Bedford and co-workers[7] that perhaps too much has been made of this association even though it occurs.

No physical signs are pathognomonic of atrial septal defect. Most commonly there is increased precordial activity, the heart is enlarged with displacement of the apex beat to the left, a moderately loud systolic murmur is heard along the left sternal border best in the first, second, and third interspaces, and the second pulmonic sound is accentuated. However, the auscultatory findings are subject to wide variation. The murmur may be louder along the lower sternal border. It has been suggested that the tricuspid valve is often dilated by the increased blood flow giving rise to a systolic murmur at the apex which is formed by the rotated enlarged right ventricle.[7] Diastolic murmurs are often heard along the sternal border or at the apex and are believed to be due to pulmonary valve incompetence and other physiologic mechanisms.[7, 18] With superimposed rheumatic heart disease typical mitral murmurs may be heard. Since theoretically a murmur caused by the defect itself should be presystolic in time, Cossio and associates[17] believe that a relative stenosis of the pulmonary ring due to dilation of the pulmonary artery and conus produces the systolic murmur. Taussig[9] believes the murmur probably originates in auricular diastole which coincides with ventricular systole. The physical findings are of even less diagnostic value in infants and there is no known way to differentiate the murmur from the systolic murmur found in patent ductus arteriosus and ventricular septal defect. Thrills are not found frequently. In the experience of others[10] thrills are rarely present in children with this anomaly. The presence of a thrill may be valuable in differentiating a high ventricular septal defect from an atrial defect in an infant. In general, there is some relationship between the intensity of the murmur, the presence of a thrill and a pulmonary diastolic murmur, to the heart size. This is in agreement with the observations of others.[15]

The electrocardiogram shows no characteristic pattern and may be normal. The frequent occurrence or right axis deviation and right ventricular hypertrophy is helpful mainly in indicating right-sided heart strain. In our experience electrocardiography is of less aid in diagnosis in infants

since right axis deviation and right ventricular preponderance may be normal findings in infancy. We have found unipolar leads of great value in demonstrating ventricular hypertrophy which is frequently difficult to determine with the standard leads alone, and we believe that no case of congenital heart disease is adequately studied without their use. Large and high P waves and prolonged P-R intervals are not infrequent but we do not feel the P waves are as characteristic as has been described in the past.[9] Delay in intraventricular conduction does not appear to be as constant a feature in children as in adults. Barber and collaborators[18] reported that 95 per cent of his patients, most of whom were adults, had right bundle branch block, and he considered the diagnosis of atrial septal defect almost untenable in its absence.

Roentgenographic and roentgenoscopic examinations are of considerable diagnostic aid since almost all cases show some type of abnormality. The typical features of enlargement of the right atrium and ventricle, dilatation of the pulmonary artery and branches, expansile pulsations of the hilar shadows, and the small aortic knob have been emphasized in the past.[6, 7, 9] Pulmonary artery dilatation is especially marked in infants. In our experience the absence of left atrial enlargement is useful in differentiating this disease from ventricular septal defect and patent ductus arteriosus in infancy. Excepting the infant group, there is in general no relationship between the heart size and general condition of the patient. Many have a greater exercise capacity than might be expected from the roentgenographic picture.

We agree with other observers[10] that in its most characteristic form the atrial septal defect in children can be diagnosed with reasonable accuracy on the basis of clinical findings including electrocardiographic and roentgen studies. However, a great problem of overdiagnosis exists. We were surprised by the great number of patients diagnosed as atrial septal defect clinically that were found by physiological studies to be suffering from another anomaly, most often a ventricular septal defect or isolated pulmonic stenosis. Accurate clinical diagnosis in infancy is extremely difficult.

Cardiac catheterization appears to be the best method of substantiating the diagnosis during life. However, the physiological data must be correlated with the clinical and roentgen observations for proper interpretation. Since surgery is now available for correction of atrial septal defects, catheterization should be used to make a more definitive diagnosis prior to contemplating operation in an individual case. The procedure is relatively easy in children but there are definite limitations to its use in infants. Use of a superficial femoral vein in often necessary in the younger age group and subsequently it becomes more difficult to enter the right ventricle and pulmonary artery. The amount of blood necessary for determining oxygen contents may be a problem. Use of microtechniques and the direct-reading cuvette, of course, can obviate this difficulty. Anesthesia is required for smaller patients and carries with it inherent risks. Because of respiratory depression with anesthesia, erroneous conclusions may be drawn from the blood sample values. We have encountered this difficulty particularly

in patients with pulmonary hypertension.

Diagnosis at catheterization is made by demonstrating a rise of oxygen content of at least 1.9 vol. per cent from superior vena cava to right atrium and by passing the catheter through the defect into the left atrium and out a pulmonary vein. It is necessary to show that a shunt occurs since the catheter may enter the left heart through a patent foramen ovale covered by a flap. By determining the oxygen saturation in the chamber into which the pulmonary vein empties one can make certain that the catheter has not entered a pulmonary vein directly from the right atrium. Observation of the catheter in the lateral view is also helpful. We have found the catheter to pass through the defect in approximately 50 per cent of cases. Clinical findings must, of course, be compatible with the diagnosis. In patients with cardiac failure there may be no evidence of left to right shunt in the right atrium and a right to left shunt may actually occur through the defect.

Other malformations can produce increased oxygen content in the right atrium. The most important of these are: (1) anomalous pulmonary veins, complete or partial, and (2) persistent atrioventricular canal or other combined atrial and ventricular defects. Anomalous pulmonary venous drainage into the right atrium may be very difficult to differentiate since this condition is usually associated with an atrial septal defect or patent foramen ovale. In the case of complete return, the peripheral arterial oxygen saturation should be the same as that in the right atrium. This is the only malformation in which the two values are both high and identical.[9] Because it is often difficult to keep younger children and infants in a stable state during catheterization, we have found it useful to obtain samples from the right atrium and femoral artery simultaneously when complete anomalous return is suspected. During the past year we have studied three infants with this anomaly. Physical and roentgenographic considerations may be valuable in differentiation. When only one or two veins return to the right atrium, diagnosis is very difficult but can be made if the catheter passes directly into the pulmonary field from the right atrium. It is worth while exploring the wall of the atrium with the catheter tip. In the case of persistent atrioventricular canal, the catheter almost always enters the left ventricle directly from the right atrium. A further increase in oxygen content over 0.9 vol. per cent may be seen in such cases and also in other combinations of atrial and ventricular defects. In view of their rarity, the following situations are usually of no great practical importance:

(1) Tricuspid insufficiency with a ventricular septal defect,[19]

(2) Arteriovenous fistula between coronary artery and coronary sinus,[20]

(3) Congenial communication between left ventricle and right atrium,[21] and

(4) Pulmonary and tricuspid insufficiency in the presence of a patent ductus arteriosus.[20]

Pulmonary hypertension in this disease is an infrequent finding in our experience. However, the three infants in whom the pulmonary artery

was entered showed a significant elevation of pulmonary pressure. This correlates well with the marked prominence of the pulmonary artery in these cases. All the patients with high pressures had severe symptoms. Keith and Forsyth[10] state that many of the children in their series of fourteen had elevated pulmonary artery pressures. In a group of twenty-five patients, eight of whom were between 5 and 14 years of age, Wood[22] found only one case with a mean pressure over 18 mm. of mercury. On the other hand, Taylor and associates[23] and Cosby and co-workers[24] found elevations in most of their patients who were of an older age group than ours. The cause of pulmonary hypertension in some patients with atrial septal defect is unknown and the subject of debate. We believe the presence of pulmonary hypertension may be of prognostic value.

Generally, angiocardiography is not necessary to demonstrate this malformation. The procedure may be useful if the right heart is seen to refill with dye coming through the defect from the left atrium. However, when dye injection is slow, dye is seen entering the right atrium late after the major portion has passed through and so may confuse the picture. The dilution factor also may make visualization of a left to right shunt difficult. Steinberg and collaborators[25] were able to show the defect only once in ten attempts. The procedure may be more worth while if the dye is forced through the defect to the left atrium by the momentary increase in right atrial pressure following rapid injection of the dye. We have attempted this in only one case (B. D., Fig. 4) and were pleased with the result. This may be more successful when the dye is injected through the

Fig. 4.—B. D., 8 months of age. Left anterior oblique angiocardiogram showing shunt of dye through atrial septal defect from right atrium.

inferior vena cava because of the relation of the septum to the orifice of this vessel. Dye may be administered directly into the right atrium through a catheter. Bailey and associates[4] state that they have been able to demonstrate the defect in a high percentage of young patients in this manner. Lind[26] finds angiocardiography with very rapid exposures in two planes valuable in diagnosis of atrial septal defect, and believes that the further development of this technique holds great promise.

The ideal method of repair of an atrial septal defect would seem to be closure of the defect under direct vision. This was attempted clinically at the University of Minnesota Hospitals twice (P. A. and S. J.) with a heart lung apparatus, but neither patient survived. Recently, closure has been successfully accomplished in three patients at this institution with the aid of hypothermia (J. J., R. G., and R. L.). The technique and the first successful case are the subject of a report by Lewis and Tauffic.[5] The postoperative course has been uneventful in all; the murmur has disappeared in two and is considerably reduced in the third. Follow-up catheterization studies have not yet been done. The surgical procedure does not appear to be difficult. Because the right atrium is dilated, there is actually an excess of atrial wall tissue, and closure of the defect therefore does not compromise atrial dynamics. Actual closure has not consumed over five minutes of time in any case.

Since surgical repair is now possible, we are faced with the problem of determining the indications for operation. At the present time we think that intervention should be reserved for those where the prognosis for the immediate future is poor. In the case of infants, the problem is great since we are often unable to determine which ones will survive the hazards of infancy and which ones will not. In any infant where the clinical condition is extremely poor and where doubts exist regarding the patient's ability to survive another episode of failure or pneumonia, we would certainly recommend surgery. When the procedure is better established and recognized as a reasonably safe one, the indications for surgical intervention will undoubtedly be considerably broadened. Since the prognosis for normal life expectancy is relatively poor, the presence of the defect itself may eventually become a justifiable indication. Our limited experience would suggest that the optimum period for this would be during childhood when the development of cardiac arrhythmias and other surgical complications is considerably less frequent than in the older individual.

Meanwhile, it is our opinion that outside of competitive sports, restrictions in activity should not be imposed on children suffering from this disease. In our experience these children limit their activities by themselves. They should be permitted to lead as normal and as active a life as possible. The psychological factors involved are extremely important. Early and adequate treatment of respiratory infections is necessary. In some, prophylactic penicillin or other antibiotics may be advisable. Prophylactic medication should always be given prior to oral surgery.

SUMMARY

Twenty-one patients were studied in whom the diagnosis of atrial septal

defect was established by cardiac catheterization. In addition, a survey was made of 202 post-mortem examinations on children with congenital heart disease, and a review made of the six cases, all infants, in whom the atrial defect appeared to be the primary cause of death.

The principal symptoms in the infants were feeding difficulties, recurrent respiratory infections, and growth retardation, and in the older children, respiratory infections, exertional dyspnea, and decreased exercise tolerance. Although children with atrial septal defect usually lead active and normal lives, the defect may lead to serious difficulty and death in infancy. Cardiac failure may occur early in life.

No cardiac signs are pathognomonic. The typical case showed increased precordial activity, displacement of the apex beat to the left, a moderately loud systolic murmur in the first, second, and third left interspaces, and an accentuated second pulmonic sound. Thrills were not frequently found. Clinical findings were more variable in the infants and accurate clinical diagnosis was extremely difficult. The poor physical development of these children was not noted as frequently as has been emphasized in the past.

No typical electrocardiographic picture occurred, but right axis deviation and right ventricular hypertrophy were frequently observed. Unipolar lead electrocardiography was found to be of great value.

Roentgenographic and roentgenoscopic examinations were of considerable diagnostic aid and typically showed enlargement of the right atrium and right ventricle, dilation of the pulmonary artery, and a small aortic knob. Pulmonary artery dilation was especially prominent in the infants. Left atrial enlargement was absent in all cases. Excepting the infant group, there was in general no relation between the heart size and general condition of the patient.

Cardiac catheterization is the best method to date of substantiating the diagnosis during life. Some of the limitations and pitfalls of this procedure are discussed. Evidence of left-to-right shunt was found in every case, and the catheter was passed through the defect in approximately 50 per cent.

Pulmonary hypertension was found infrequently but was a fairly consistent finding in the catheterized infants. In no case was the hypertension of a severe nature.

Three cases have undergone successful surgical closure of the atrial defect at the University of Minnesota Hospitals. The indications for surgery are discussed briefly as in the clinical management of children with this type of cardiac defect.

Stress is placed on early diagnosis of this anomaly since the development of surgical treatment may make possible the salvage of infants who would otherwise die.

REFERENCES

1. Murray, G.: Closure of Defects in Cardiac Septa, Ann. Surg. **128:** 992, 1948.
2. Swan, H.: Surgical Closure of Interauricular Septal Defects, J. A. M. A. **151:** 792, 1953.
3. Gross, R. E.: Surgical Closure of Interauricular Septal Defects, J. A. M. A. **151:** 795, 1953.
4. Bailey, C. P., Downing, D. F., Geckeler, G. D., Likoff, W., Goldberg, H., Scott, J. C., Janton, O., and Redondo-Ramirez, H. P.: Congenital Interatrial Communications: Clinical and Surgical Con-

siderations With a Description on a New Surgical Technic: Atrio-septpexy, Ann. Int. Med. **37**: 888, 1952.
5. Lewis, F. J., and Tauffic, M.: Closure of Atrial Septal Defects With the Aid of Hypothermia; Experimental Accomplishments and the Report of One Successful Case, Surgery **33**: 52, 1953.
6. Roesler, H.: Interatrial Septal Defect, Arch. Int. Med. **54**: 339, 1934.
7. Bedford, D. E., Papp, C., and Parkinson, J.: Atrial Septal Defect, Brit. Heart J. **3**: 37, 1941.
8. Taussig, H. B., Harvey, A. M., and Follis, R. H., Jr.: Clinical and Pathological Findings in Interauricular Septal Defects; a Report of Four Cases, Bull. Johns Hopkins Hosp. **63**: 61, 1938.
9. Taussig, H. B.: Congenital Malformation of the Heart, New York, 1947, Commonwealth Fund.
10. Keith, J. D., and Forsyth, C. C.: Auricular Septal Defects in Children, J. PEDIAT. **38**: 172, 1951.
11. Cournand, A., Baldwin, J. S. and Himmelstein, A.: Cardiac Catheterization in Congenital Heart Disease, New York, 1949, Commonwealth Fund.
12. Van Slyke, D. D., and Neill, J. M.: Determination of Gases in Blood and Other Solutions by Vacuum Extraction and by Manometric Measurement, J. Biol. Chem. **61**: 533, 1924.
13. Dexter, L., Haynes, F. W., Burwell, C. S., Eppinger, E. C., Sagerson, R. P., and Evans, J. M.: Studies in Congenital Heart Disease. III. The Pressure and Oxygen Content of Blood in the Right Atrium, Right Ventricle and Pulmonary Artery in Control Patients With Observations on the Oxygen Saturation and Source of Pulmonary Capillary Blood, J. Clin. Invest. **26**: 554, 1947.
14. Kroop, I. G., Steinberg, M. F., and Grishman, A.: The Nature of Left Axis Deviation in Congenital Cardiac Defects With Right Ventricular Hypertrophy, Am. Heart J. **41**: 891, 1951.
15. Cosby, R. S., and Griffith, G. C.: Interatrial Septal Defect, Am. Heart J. **38**: 80, 1949.
16. Abbott, M. E.: Atlas of Congenital Heart Disease, New York, 1936, American Heart Association.
17. Cossio, P., Arana, R. S., Berconsky, I., and Kreutzer, R.: Semana méd. **2**: 364, 1938.
18. Barber, J. M., Magidson, O., and Wood, P.: Atrial Septal Defect With Special Reference to the Electrocardiogram, Pulmonary Artery Pressure, and Second Heart Sound, Brit. Heart J. **12**: 277, 1950.
19. Baldwin, E. de F., Moore, L. V., and Noble, R. P.: The Demonstration of Ventricular Septal Defect by Means of Right Heart Catheterization, Am. Heart J. **32**: **152**, 1946.
20. Holling, H. E., and Zak, G. A.: Cardiac Catheterization in Congenital Heart Disease, Brit. Heart J. **12**: 153, 1950.
21. Perry, E. L., Burchell, H. B., and Edwards, J. E.: Congenital Communication Between the Left Ventricle and the Right Atrium: Co-existing Ventricular Septal Defect and Double Tricuspid Orifice, Proc. Staff Meet., Mayo Clin. **24**: 198, 1949.
22. Wood, P.: Congenital Heart Disease. A Review of Its Clinical Aspects in the Light of Experience Gained by Means of Modern Techniques, Brit. M. J. **2**: 639, 693, 1950.
23. Taylor, B. E., Geraci, J. E., Pollock, A. A., Burchell, H. B., and Wood, E. H.: Interatrial Mixing of Blood and Pulmonary Circulatory Dynamics in Atrial Septal Defect, Proc. Staff. Meet., Mayo Clin. **23**: 500, 1948.
24. Cosby, R. S., Griffith, G. C., Zimm, W. J., Levinson, D. C., Dimitroff, S. P., Oblath, R. W., and Jacobson, G.: Cardiac Catheterization in Interatrial Septal Defect, Am. J. Med. **14**: 4, 1953.
25. Steinberg, M. F., Grishman, A., and Sussman, M. D.: Angiocardiography in Congenital Heart Disease. II, Intracardiac Shunts, Am. J. Roentgenol. **49**: 766, 1943.
26. Lind, J.: Personal communication.

A FOLLOW-UP STUDY OF SUSPECTED RHEUMATIC FEVER PATIENTS

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IT MAY be very difficult to evaluate a small group of patients having symptoms and signs suggestive of rheumatic fever but not truly diagnostic. In the Medical College of Virginia Rheumatic Fever Clinic where 2,678 new patients have been referred for study from 1941 through 1952, 236 have been deferred as to diagnosis at the time of the initial visit. A follow-up study of this group shows their later diagnosis, and the time they were followed. It is the purpose of this paper to discuss the reason for deferral and to confirm the major initial findings on the few who later were clarified as rheumatic fever with the group as a whole. The types of rheumatic heart disease later found will be listed. It is hoped that such a study will be of value to clinicians trying to clarify such a diagnosis as early in the illness as possible.

HISTORICAL

The long-term follow-up studies by Bland and Jones,[1] Ash,[2] and Wilson and Lubschez[3] give credence to the fact that those without clearly demonstrable heart disease in or after the first attack of rheumatic fever do better over a period of years than those with carditis. But no follow-up studies on the suspected or deferred cases could be found.

Strict diagnostic criteria have been emphasized by T. D. Jones[4] and Taran[5] as well as many others. But several types of vague symptoms have caused honest doubt in the minds of the examiners. "Growing pains" if they are purely muscular and at night in an otherwise well child may be no problem. With joints also involved with pain, even without heat, there may be doubt. Shapiro,[6] in 1939, compared such pains with pains of rheumatic fever.

A suspicious murmur, but one not clearly due to mitral insufficiency, may be the reason for deferral. Shapiro[7] has followed 102 patients with nonpathologic murmurs and no history of rheumatic fever, and in 98 per cent he felt the diagnosis was later correct.

MATERIAL AND METHOD

The Richmond Rheumatic Fever Clinic has seen patients by referral only from physicans throughout Virginia for over eleven years. All patients were suspected of having rheumatic fever or heart disease and were less than 20 years of age. A total of 2,678 new patients had been seen prior to Jan. 1, 1953. A previously reported study of this group showed

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that about one-half were confirmed as rheumatic fever.[8]

This study is concerned with 236 patients on whom a "deferred" diagnosis was made at the time of the initial visit. Each patient had a complete medical history, physical examination, complete blood count, urinalysis, flocculation, sedimentation rate, vaginal smear, stool examination, sickling test (Negroes only), electrocardiogram, and chest roentgenogram. Each was seen by at least one pediatrician and a cardiologist. Special studies were ordered where indicated. In this group, after careful study, we did not feel that a clear diagnosis of rheumatic fever could be made, nor could they be immediately dismissed as no heart disease. A diagnosis of rheumatic fever was not made without clear evidence of a major manifestation.

Of the 236 patients with a deferred diagnosis, reports are available for later scrutiny on 209. In twenty-seven no further information could be obtained.

Table I Column A lists the leading symptoms and signs that led this indefinite group of 236 patients to a physician. In each case the two or three major initial complaints were noted, as well as any physical or laboratory features which suggested possible carditis. Table I Column B lists the same for the twenty-nine who were later confirmed as having rheumatic fever.

TABLE I. REASONS FOR INITIAL DEFERRAL

SYMPTOMS AND SIGNS	A TOTAL DEFERRED GROUP 236 PATIENTS	B CONFIRMED AS RHEUMATIC FEVER 29 PATIENTS
Aches in extremities	134	15
Aches with swelling in joints	30	7
Fever	97	14
Fatigue	51	7
Abdominal pain	34	1
Nervousness	33	3
Frequent URIs	30	6
Epistaxis	21	4
Weight loss	17	2
Family history of rheumatic fever	12	1
Suspicious choreiform movements	11	4
Headache	8	1
Chest pain	8	0
Rash	4	0
Nodules	3	0
Increased sedimentation rate	37	7
Suspicious of abnormal electrocardiogram	29	9
Suspicious murmurs	83	12
Suspicious x-ray, size, or contour	40	4
Tachycardia	23	5
Abnormal sounds including arrhythmia	9	0

TABLE II. FINAL DIAGNOSES

	NO. CASES	PER CENT
Rheumatic fever	29	13.88
No rheumatic fever or heart disease on recheck in our clinic	140	66.98
Local medical doctor says no rheumatic fever or heart disease	19	9.09
Public health nurse says patient well	8	3.83
Still deferred after recheck	13	6.22
Total cases followed	209	
Not rechecked	27	
Total deferred	236	

The final diagnoses are shown in Table II. While only 66.98 per cent were demonstrated to be without rheumatic infection in our clinic, we believe that those rechecked by their local physicians and nurses bring the total without rheumatic fever to 79.9 per cent. In nineteen cases we were dependent on local physicians for the report of no rheumatic fever or rheumatic heart disease as no return to

the clinic was possible. In eight we have nurses' reports that the patients appear well. This is not entirely satisfactory, but it has value when added to 140 patients who did return and were found free of rheumatic fever.

There were thirteen cases rechecked and still classified deferred. All except three of these have been followed less than 7 months and need further observation. The average follow-up period of this group is 14.5 months.

The detailed times of following each group are shown in Table III. The average of all is 28 months. The 79.9 per cent listed as nonrheumatics were followed on the average slightly over 24 months.

murmurs can now be detected. No deaths have occurred so far in the 209 followed.

DIFFERENTIAL DIAGNOSIS

Among the final diagnoses on the many "noncardiacs" we find the chief problems in differential diagnosis. These diagnoses emerged after further study:

1. Infections outside the heart as recurrent tonsillitis, bronchitis, cervical adenitis, pyuria, gonorrhea, dental abscess, nephritis, infectious mononucleosis and osteomyelitis, syphilis, and tuberculosis. (In eleven cases the patient seemed to be well after tonsillectomy and adenoidectomy.)

TABLE III. DIAGNOSIS AND TIME OF OBSERVATION

TIME FOLLOWED	RF* CONFIRMED	RECHECK AND NO RF OR HEART DISEASE	LOCAL DOCTOR REPORTS NO RF OR HEART DISEASE	NURSES SAY PATIENT WELL	RECHECK, STILL DEFERRED
0-3 mo.	1	7	–	1	3
3-6 mo.	–	10	2	2	4
6-12 mo.	2	29	4	2	3
1-2 yr.	6	35	2	1	1
2-4 yr.	6	39	6	1	1
4-6 yr.	6	16	3	–	1
6-8 yr.	5	4	2	–	
8-10 yr.	3	–	–	1	
Total	29	140	19	8	13

*Rheumatic fever.

The twenty-nine patients who later developed explosive or clear signs of rheumatic fever have been followed for an average of 47 months. Only five patients have residual heart damage, or 2.4 per cent of the deferred cases followed. Four have mitral insufficiency without enlargement. One has both mitral and aortic insufficiency without enlargement. Five more cases had mitral valvulitis with a typical murmur of mitral insufficiency during the acute stage, but no

2. Congenital defects as ectopic kidney, diverticulum of the stomach, hypothyroidism, epilepsy, congenital orthopedic defects of legs and mental deficiency.

3. Allergies.

4. Parasites.

5. Psychoneurosis and neurocirculatory asthenia.

6. Malnutrition.

7. Tumors.

CONCLUSION

1. In the past eleven years 2,678 new patients have been seen in the Medical College of Virginia Rheumatic Fever Clinic. In this group, 236 were listed as "deferred" after a complete initial study. Follow-up data have been obtained on 209 of these 236 cases.

2. The complaints and suspicious signs which were the reason for deferral in the total group are listed and compared with those later developing clear rheumatic fever.

3. After an average follow-up period of 28 months, the following diagnoses have emerged:

Rheumatic fever (2.4% with rheumatic heart disease)	13.88%
Rechecked and no rheumatic fever or heart disease found	66.98%
Local medical doctor says no rheumatic fever	9.09%
Nurse says patient well	3.83%
Diagnosis still deferred after recheck	6.22%

4. The excellent prognosis in this group as a whole makes strict diagnostic criteria imperative.

The author wishes to thank Dr. Louise Galvin, Director of the Virginia Crippled Childrens Bureau, for her assistance in establishing the clinic, serving as clinical director until 1947, and making records available. The many nurses and social workers who helped to trace cases have rendered invaluable assistance.

REFERENCES

1. Bland, E. F., and Jones, T. D.: A 20 Year Report on 1,000 Patients Followed Since Childhood, Circulation **4**: 836, 1951.
2. Ash, Rachel: The First Ten Years of of Rheumatic Infection in Childhood, Am. Heart J. **36**: 89, 1948.
3. Wilson, M. G., and Lubschez, R.: Longevity in Rheumatic Fever: Based on the Experience of 1,042 Children Observed Over a Period of Thirty Years, J. A. M. A. **138**: 749, 1948.
4. Jones, T. D.: The Diagnosis of Rheumatic Fever, J. A. M. A. **126**: 481, 1944.
5. Taran, L. M.: The Clinical and Laboratory Diagnostic Criteria of Rheumatic Fever in Children, Am. J. Med. **2**: 368, 1947.
6. Shapiro, M. J.: Differential Diagnosis of Non-rheumatic "Growing Pains" and Subacute Rheumatic Fever, J. PEDIAT. **14**: 315, 1939.
7. Shapiro, M. J.: Follow-up Study of Systolic Murmurs, Am. Heart J. **17**: 416, 1939.
8. McCue, C. M., and Galvin, L. F.: A Preliminary Report on Rheumatic Fever in Virginia, J. PEDIAT. **33**: 467, 1948.

GRAPE JUICE IN INFANT FEEDING

Comparative Sensitivity to Orange and Grape

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ONE of the problems that frequently vexes the mother and the pediatrician is that of giving added fluids in warm weather or of forcing fluids during illnesses in small infants and children. Plain water is more often rejected than not. The difficulty can occasionally be surmounted in the home on a short-term basis by offering sweetened water, weak tea, carbonated beverages, or diluted fruit juices. None of these measures is entirely satisfactory, particularly with younger infants. In an institution, the problem is naturally more acute. Unlike the mother with one or possibly two children whose fluid balance must be maintained, the nurses in institutions have from six to twelve charges with a limited amount of time to spend on this particular task. The result is that, added to acute infection from which the child may be suffering, we frequently have the complication of dehydration and acidosis. While in the home the mother may test a variety of liquids for acceptability, in an institution caring for several hundred infants and children this is a practical impossibility.

Acceptability is an important factor, not only to the sick child, but also to the well child whose afternoon "added nourishment" is frequently a high light of the day. Among the beverages we have tested over a short-term and long-term period is grape juice. We were agreeably surprised with this drink from the point of view of acceptability in all of the small number of infants and children first observed. We were also interested in observing that several of our allergic infants who could not tolerate orange juice could drink grape juice with impunity. Accordingly, we thought that a more exhaustive study on acceptability and tolerance was warranted.

The problem of allergy to orange juice is an old one in pediatrics and one which is by no means solved. Most pediatricians have had experience with the eczematous infant who is unable to tolerate orange juice without an exacerbation of his eczema. While this is a well-known clinical fact, there is very little data available in the literature on sensitivity to orange juice. It was thought that some contribution might be made to this problem by skin testing a reasonably large number of infants and children with orange and grape antigens. Since skin testing alone is not invariably accurate, challenge feeding with these substances was also employed.[1, 2, 3, 4]

CLINICAL PLAN

The clinical material was comprised of infants and children in residence at the New York Foundling Hospital, as well as those infants and children who attended our outpatient clinic. The latter represent children who are boarded out in foster homes and who continue as charges of the institution until their eighteenth year, unless they are returned to their own homes. Many

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of these children were formerly in residence at the Foundling Hospital, and the large majority had been followed consecutively in the clinic for long periods of time by a stable clinic personnel. Their medical histories could therefore be considered quite reliable and complete. The infants in residence at the Foundling Hospital represented a group from birth to 2 years of age who were awaiting social disposition. While most of these infants were admitted as well, they naturally acquired the usual range of illnesses, infections, gastrointestinal disorders, eczema, etc., incident to their age group and also to the fact that they were maintained in the congregate.

Observations on acceptability of the grape juice were confined to the infants in the institution, since this group was under direct care and because the reactions of most of them to oral feeding with orange juice were already known.* All of the infants were given daily offerings of diluted grape juice. Infants up to one year were offered 2 to 4 ounces of one-third diluted grape juice; infants over one year were offered 4 to 6 ounces of one-half diluted grape juice. Records were kept on acceptability, gastrointestinal reactions such as vomiting, diarrhea, etc., and on possible skin reactions. This part of the study was continued for a period of about three months.

Intradermal skin testing was performed on all infants over 6 months of age in the institution, and on all available clinic cases with the sole ex-

*The grape juice was supplied by The Welch Grape Juice Company, and was prepared exclusively from Concord grapes.

TABLE I. OBSERVATIONS ON ACCEPTABILITY

AGE GROUP	TIME ON GRAPE JUICE				TOTAL
	0-1 WK.	1 WK.-1 MO.	1-2 MO.	2-3 MO.	
0.3 mo.*	0	22	0	0	22
2-8 mo.†	7	10	3	0	20
4-9 mo.	4	41	21	13	79
6 mo.-1 yr.	1	26	14	37	78
1-1½ yr.‡	9	28	8	0	45
13-20 mo.	2	10	12	15	39
18-20 mo.	3	7	12	25	47
1½-2½ yr.§	5	7	6	9	27
Miscellaneous (Medical Floor)	2	3	0	3	8
Total	33	154	76	102	365

*Six discontinuances.
†Two discontinuances.
‡One discontinuance.
§Three partial discontinuances.

TABLE II. INTRADERMAL REACTIONS BY AGES (379 PATIENTS)

AGE (YEARS)	ORANGE								GRAPE							
	1:1,000				1:500				1:1,000				1:500			
	0	±	+	++	0	±	+	++	0	±	+	++	0	±	+	++
½-1	100	5	1		100	5	1		101	5			103	2*		1
1-1½	69	1			68	2			69				68	1	1	
1½-2	33	3			35	1			35		1		36			
2-4	39	1	1		51				49	2			50	1		
4-6	18	1			19				17	2			19			
6-10	30				30				29		1		29		1	
10+	67				66	1			66	1			67			
Total	366	11	2		369	9	1		366	10	2		372	4	2	1

*One case also in 1:1,000 dilution—negative to orange juice.

TABLE III. POSITIVE INTRADERMAL REACTORS*

NO.	CASE	SEX	HISTORY OF ALLERGY	AGES (YR.	MO.)	ORANGE 1:1,000 ±	+	++	ORANGE 1:500 ±	+	++	GRAPE 1:1,000 ±	+	++	GRAPE 1:500 ±	+	++
1	B. B.	F	None		6				x						x		
2	R. A.	M	None		6				x								
3	M. R.	M	None		7				x								
4	A. A.	F	None		7					x							
5	G. A.	M	None		7												
6	P. A.	F	None		7							x			x		
7	R. T.	M	None		8				x								
8	L. T.	F	None		8				x			x					
9	S. F.	F	None		8							x					
10	B. L.	M	None		9		x										
11	P. G.	F	None		9							x					
12	J. T.	F	None		10	x											
13	M. N.	F	None		10												x
14	F. S.	M	None		10	x											
15	P. R.	M	Eggs		10	x											
16	A. R.	F	Contact dermatitis	1		x						x					
17	E. I.	M	None	1	2										x		
18	E. E.	F	None	1	2	x											
19	E. M.	M	None	1	3				x								
20	R. P.	M	None	1	3											x	
21	L. R.	F	None	1	2				x								
22	M. H.	M	None	1	11	x											
23	I. L.	F	Eczema	2		x							x				
24	D. C.	M	Eczema	2		x											
25	M. T.	F	Orange juice	2					x								
26	Z. C.	F	None	2	3							x					
27	B. C.	F	None	2	6		x										
28	B. G.	F	None	4		x											
29	A. D.	F	None	1		x											
30	H. R.	F	None	3													
31	M. C.	F	None	3	6										x		
32	R. L.	F	None	4	6							x					
33	A. S.	M	None	7								x					
34	J. W.	M	None	9												x	
35	R. C.	F	None	12									x				
36	W. Y.	M	None	16					x			x					
37	R. G.	F	None	6		x						x					
Total						11	2		9	1		10	2		4	2	1

*All negative to oral challenge.

ception of actively eczematous infants. Such infants were challenged orally. Each infant or child received four intradermal tests, two for orange and two for grape, simultaneously, two on the flexor surfaces of each arm. The amount for each test was 0.01 c.c. and each antigen was tested in 1:1,000 and 1:500 dilution.* Readings were taken twenty minutes after injection and recorded in the following manner: negative; plus-minus, 0 to 5 mm. in diamter; one plus, 5 to 10 mm.; two plus, 10 to 12 mm. All positive reactors were subsequently challenged orally.

RESULTS

Table I depicts the results obtained on acceptability. Of all infants tested, 356 out of 365 (97.6 per cent) accepted the daily offerings of grape juice for periods ranging from one week to three months. In only nine instances (2.4 per cent) was it necessary to completely discontinue the use of the product, six because of persistent refusal and three because of gastrointestinal upsets, chiefly vomiting. Three infants with chronic eczemas were included in these observations; all of them were unable to tolerate orange juice in any quantity. Two of these infants were able to tolerate grape juice for eight days without exacerbation of skin pathology and one infant continued in the study for the full three months when given grape juice every other day.

A total of 1,516 skin tests were performed on 379 cases; 192 males and 187 females. Table II gives the results of these tests in age groups, and it will be noted that no instances of three plus or four plus reactions occurred. The incidence of negative reactions to grape was 95.3 per cent and to orange 94 per cent. Eighteen cases (4.7 per cent) gave positive reactions to grape, and twenty-three (6 per cent) gave positive reactions to orange. These differences are of no importance statistically. A more detailed analysis of the positive reactions is given in Table III. Four infants reacted both to orange and grape antigen, but did not react clinically to oral challenge; two of these were known atopic individuals—contact dermatitis and an old asymptomatic eczema. A 2-year-old positive reactor to orange juice with a verifiable past history of intolerance to orange juice gave no reaction to oral challenge at the time these tests were undertaken. Among the negative reactors to both orange and grape, there were twenty-one who had positive allergic histories (Table IV). None of these reacted clinically to grape, but two of the infants with histories of intolerance to orange juice still responded clinically to the administration of this antigen by mouth.

TABLE IV. NEGATIVE INTRADERMAL REACTORS

Positive Allergic History	
Eczema (infancy)	3
Contact dermatitis	6
Seborrheic dermatitis	1
Drugs	2
Orange juice	7
Eggs	1
Multiple	1
Total	21

DISCUSSION

In practically all instances, grape juice was acceptable to the infants tested, not only on a short-term basis, but also on a long-term day-to-day

*The antigens were obtained from the Hollister-Stier Laboratories of Philadelphia, Pa. The protein extract of grape was composed of a mixture of Concord, Muscat, Tokay, and Thompson grapes.

testing. Even infants as young as 2 weeks of age accepted grape juice well. It should be pointed out that the fluid was not forced, but simply offered. The long-term acceptance was noteworthy, since our experiences with other fruit juices in this particular have been disappointing. Because of its general acceptance, we found also that grape juice served as a useful vehicle for poorly accepted medications and we have frequently utilized it for this purpose.

Our experiences with the intradermal reactions parallel those of other observers, and are interesting chiefly because of their negative value.[1, 2, 3, 4] Since we were not dealing exclusively with an allergic group of infants and children, our incidence of positive reactions did not approximate the findings of Criep[5] or of Hill.[6] There was no correlation between positive intradermal reactions and clinical reactions. The converse was also true—negative intradermal reactions did not reflect clinical findings. It may be that intradermal reactors were not present in this group in numbers large enough to give us conclusive information. On the other hand, it is also possible that clinical findings might have correlated somewhat better had we had a series of three plus or four plus intradermal reactors. This did not occur. There was no noticeable difference between grape and orange in the frequency of positive intradermal reactions. However, no clinical reactions could be ascribed specifically to grape and, in the few trials available, grape showed less of a tendency to exacerbate eczema than did orange. The intradermal grape antigen was composed of a number of different types of grape while the product used for oral challenge was exclusively Concord grape. In view of the paucity of grape reactors and the fact that their reactions were slight, we do not feel that any further information would have been obtained by preparing an antigen specific to the Concord grape.

CONCLUSIONS

1. Grape juice was acceptable as a daily routine for periods ranging from one week to three months in 97.6 per cent of 365 infants tested. None of the infants receiving grape juice showed any allergic manifestations.

2. Three hundred seventy-nine infants and children were tested intradermally with 1:1,000 and 1:500 dilutions of grape and orange. Only eighteen cases (4.7 per cent) gave positive reactions. Twenty-three cases (6 per cent) gave positive reactions to orange.

3. There was no correlation between positive intradermal reactions and positive clinical reactions.

4. Under the conditions of this investigation, positive clinical findings are a more significant index of sensitivity than positive intradermal reactions.

5. Grape juice was found to be a highly convenient vehicle for administering poorly accepted medications.

REFERENCES

1. Randolph, T. G.: Management of Food Allergy, M. Clin. North America **32**: 245, 1948.
2. Walbott, G. L., Shea, J. J., and Harrington, M. M.: Adequate Diets in Advanced Chronic Asthma, Am. Allergy **6**: 572, 1948.
3. Taft, L.: Clinical Evaluation of Skin Tests, J. Allergy **11**: 335, 1943.
4. Liebowitz, H., Chester, Alexander, and Markow, H.: J. A. M. A. **144**: 990, 1950.
5. Criep, Leo H.: Essentials of Allergy, Pittsburgh, 1945, J. B. Lippincott Co.
6. Hill, L. W.: Food Sensitivity in 100 Asthmatic Children, New England J. Med. **238**: 657, 1948.

BACTERIOLOGIC AND CLINICAL INTERPRETATION OF THE FLORA OF THE NOSE AND NASOPHARYNX IN CHILDREN

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DISORDERS of the nose and pharynx (which includes the nasopharynx) constitute a large part of illness encountered in pediatric practice. Nasal symptoms, occasionally associated with cough and other systemic manifestations, often develop into protracted and difficult problems which fail to respond to a variety of medications and regimens. The reason can usually be found in the fact that too often upper respiratory complaints are treated without exact knowledge of the underlying disease. The determination whether an infectious or noninfectious process exists is of prime importance in the management of rhinologic disorders.

In children as in adults, many nasal problems have as their basis a vasomotor rather than an infectious disturbance. In this respect the term "vasomotor" is used in its broad sense. Not only specific allergens but physical, emotional, and constitutional factors as well as the local use of medications may be responsible for rhinitis or sinusitis with the production of secretion and nasal obstruction and other attendant symptoms. If an infectious process is present, the most effective application of therapy depends on knowledge of the infecting agent. One should also know whether the source of infection is the adenoid tissue in the nasopharynx or the paranasal sinuses.

A good deal of the information obtained from the usual rhinologic investigation lacks precision. Direct examination of the nasal cavities, transillumination, and even roentgenograms present data which at best are only suggestive. It should be emphasized at this point that the finding of secretion per se in the nose, regardless of amount or appearance, does not necessarily mean that infection is present. More often it indicates an abnormal vasomotor response. A procedure of diagnostic value is lavage of the maxillary antrum. Irrigation of the antrum through the natural orifice is very simple in a cooperative child. But here again the secretion obtained offers suggestive but not definitive information.

Thus, it is obvious that there is great need for more specific criteria in diagnosis and treatment of nasal and sinus disease. If these criteria can be acquired simply in children, the advantages are further enhanced since the obstacle most frequently met is lack of cooperation. The fact is that they can be obtained by bacteriologic and cytologic study of nasal and sinus secretions. In this way the differential diagnosis between infectious and noninfectious (vasomotor)

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disorders can be established, and the infecting agent may be identified as well as its susceptibility to antibiotics estimated.

The bacteriologic criteria which have been developed are largely based upon comparative bacteriologic study of the flora of the nose and nasopharynx in health and disease in adults.[1] Deductions from the data accumulated have proved to be most valuable in our hands during the past six years. The following study was undertaken to determine whether the bacteriologic findings in children are similar to those which were obtained in adults.

Fifty children between 4 and 12 years of age were chosen as subjects for this study. These children had been admitted to the Pediatric Service at The Mount Sinai Hospital during the winter and spring months for illnesses which did not affect the respiratory tract. In addition to the history, absence of respiratory disease was established by direct examination of the upper respiratory tract and by transillumination of the maxillary antrums. A previous tonsillectomy and adenoidectomy had been performed on twenty of the children. Cultures of the nasal cavities were made by passing a platinum loop over the middle and inferior turbinates and inoculating the collected material on blood agar plates. Cultures of the nasopharynx were made similarly by passing a curved large platinum loop into the nasopharynx. The latter procedures were executed under direct vision, avoiding contact of the loop with the mouth or pharynx.[2]

The technique described here avoids the combined culture of the nose and nasopharynx which is usually inevitable when a cotton swab is used. The cotton swab method is undesirable in that it often provokes gagging when placed in the inferior meatus, which frequently brings nasopharyngeal secretion into the inferior meatus posteriorly.

TABLE I. FLORA OF NORMAL NOSE AND NASOPHARYNX (50 CHILDREN)

	NOSE	NASOPHARYNX
Pneumococcus	0	1
Streptococcus hemolyticus	0	1
Streptococcus viridans	0	30
Streptococcus nonhemolyticus	0	0
Staphylococcus aureus		
A	8	5
B	0	0
Staphylococcus albus		
A	0	0
B	21	31
Diphtheroids	2	3
Neisseria pharyngis	7	34
No growth	16	0
Total	54	105

The findings in our study of this group of children are similar to those which were obtained in normal adults (Table I). Microorganisms such as pneumococci, alpha and beta hemolytic streptococci, *Hemophilus influenzae* and *parainfluenzae*, and *Klebsiella pneumoniae* were not found in normal nasal cavities. *Staphylococcus aureus* A (pathogenic variety) was obtained in eight instances. However, the number of microorganisms was very small and they were not present in significant numbers on microscopic examination of the secretion (spreads). This finding is also consistent with that obtained in adults. The predominant nonpathogen was *Staphylococcus albus* B. The large number of sterile cultures, sixteen, should be noted.

In contrast to these findings, many nasopharyngeal cultures showed the presence of a variety of microorgan-

isms. A pneumococcus and a *Streptococcus hemolyticus* each were isolated once (2 per cent as compared to 21 per cent and 18 per cent, respectively, in adults), while *Streptococcus viridans* was recovered in thirty instances (60 per cent as compared to 35 per cent in adults). The small number of pneumococci and hemolytic streptococci in the nasopharynx in this series is noteworthy. Possibly the incidence of hemolytic streptococci might have been higher if a selective medium such as Pike's medium had been used. However, the presented study is a fair appraisal.

In this series the twenty children with previous tonsillectomy and adenoidectomy showed no significant difference in nasopharyngeal flora.

TABLE II. FLORA OF NASAL INFECTIONS (50 CHILDREN)

Pneumococcus	23
Streptococcus hemolyticus	5
Streptococcus viridans	7
Streptococcus nonhemolyticus	0
Staphylococcus aureus	
A	20
B	5
Staphylococcus albus	
A	1
B	3
Hemophilus influenzae	1
Hemophilus parainfluenzae	9
Diphtheroids	17
Neisseria pharyngis	15
Coli-aerogenes	1
Total	107

To compare the nasal flora among children suffering from nasal infections, fifty patients whose bacteriologic and cytologic findings satisfied our criteria for infections are presented (Table II). Briefly, these criteria required (1) the isolation of microorganisms such as pneumococci, any streptococci (particularly alpha and beta hemolytic), *H. influenzae* and *parainfluenzae, K. pneumoniae* in any numbers, and *Staph. aureus* A in moderate to large numbers from cultures of the nasal or sinus secretion, and (2) the finding of these microorganisms in appreciable numbers on microscopic examination of the same secretion spread on slides.[2] These patients were studied in the outpatient department of The Mount Sinai Hospital and in private practice. The large number of pneumococci (46 per cent) and *Staph. aureus* A (40 per cent) in these nasal secretions is significant, especially since similar findings have been obtained by us in adults. *Str. hemolyticus* was isolated in 10 per cent of the cases and *Str. viridans* in 14 per cent. The comparatively large percentage (18 per cent) of *H. parainfluenzae* suggests that this microorganism is not an uncommon pathogen.

In some nasal cultures, microorganisms of the *Neisseria pharyngis* group and diphtheroids were also found in large numbers. When such combinations are isolated from secretion from the posterior regions of the nasal cavities, it may be considered that the source of the original infection is in the nasopharynx.

The nasopharynx was cultured in one-third of these cases. In most instances the microorganism isolated from the nose was also cultured from the nasopharynx.

COMMENT

Infection of the nose or sinuses implies active multiplication of bacteria in these areas. In the nose and sinuses, infections begin on the surface. Thus, if infection is present, it should be expected that microscopic examination of nasal and sinus secretion should reveal the presence of micro-

organisms. The information obtained from the spread of nasal or sinus secretion should be used in correlation with cultural findings. Suffice it to state here that the finding of significant microorganisms (i.e., pneumococci, alpha and beta hemolytic streptococci, *H. influenzae* and *parainfluenzae, K. pneumoniae, Staph. aureus* A in moderate numbers) in nasal secretion on culture with the presence of appreciable numbers of the same microorganism on the spread indicates the existence of infection. On the other hand, the isolation on culture of a nonsignificant microorganism (i.e., *Staph. albus* and *aureus* B, especially in small numbers, *Staph. aureus* A in small numbers, diphtheroids, *Neisseria pharyngis*) and the absence of these microorganisms on the spread point to a noninfectious disturbance. This is particularly true if large amounts of mucus and mucus threads are detected on the spread. Such findings would suggest a vasomotor disorder. The routine Wright stain is used for microscopic examination of secretion.

The basic facts gained from our various studies on this subject permit conclusions which can have valuable clinical application. The normal nose is usually free from pathogenic bacteria and the number of bacteria which may be present are very small. With good technique, sterile cultures are obtained from the nose not infrequently. This speaks for the effectiveness of the natural antibacterial substance lysozyme present in nasal mucus and the ciliary action which propels material in the nose toward the nasopharynx.

The nasopharynx, on the other hand, does harbor potential pathogenic bacteria under normal conditions and is the carrier-focus of bacteria for the respiratory tract. When the antibacterial defenses of the nose and laryngotracheobronchial tree break down, pathogenic microorganisms from the nasopharynx spread into these areas and cause disease. As a matter of fact, the flora of the nasopharynx may have clinical significance without local manifestations of disease, particularly in the field of focal infection. Under clinical conditions it is very difficult to determine where normalcy stops and infection of the nasopharynx begins. It is likely that some nasopharyngeal infections spread into the nose, particularly in children, because the virulence of the infection overpowers the protective barriers of the nose. In other instances, the protective mechanism may be inhibited by viral infections or chilling or fatigue and thus enable potential pathogens in the nasopharynx to spread forward without local resistance.

In this connection, the local use of nonirritating antibiotics in the nose before full invasion of bacteria into the nose occurs may be of value. In other words, the antibiotic helps to reinforce the nasal resistance against the forward migration of the nasopharyngeal flora. This may be especially helpful in those patients who are prone to develop a severe suppurative stage after the onset of a coryza.

SUMMARY AND CONCLUSION

As in adults, the nasal flora in this study of fifty normal children contained chiefly nonpathogenic microorganisms in small numbers. *Staph. albus* B was present most frequently. The large number of sterile cultures obtained from normal noses is signifi-

cant. The only potential pathogen found in normal nasal secretion with regularity is the *Staph. aureus* A. The number of microorganisms detected in spreads in such instances is very small. This is contrary to the finding in infections.

On the other hand, potential pathogens may be present in the nasopharynx of normal children. The one encountered most frequently in this series was *Str. viridans*. Although the pneumococcus and *Str. hemolyticus* were isolated each once, the percentage in a similar series of adults was much higher (21 and 18 per cent, respectively, from a series of 146 adults). The large number of Neisseria species should be expected. There was no sterile culture in this group.

A study of the flora of fifty children with nasal infections revealed mainly the presence of pathogens. These were usually found in appreciable numbers on spreads.

It should be noted that pathogens were isolated in sixty-five instances from a total of 107 microorganisms obtained in the fifty cases. As has been found in adults, pneumococcus and *Staph. aureus* A were the most common. The comparatively large number of *H. parainfluenzae* should be of interest. Once again, this series shows that *Str. hemolyticus* is not as omnipresent in upper respiratory infections, or in the normal nasopharynx for that matter, as is usually thought.

These as well as other studies made by us strongly suggest that the nasopharynx in health harbors or might be considered the carrier-focus of pathogens or potential pathogenic microorganisms. These microorganisms spread into the nose and sinuses, or into the laryngotracheobronchial tree, to cause disease when the defensive antibacterial barriers are broken by lowered tissue resistance or other disease processes.

REFERENCES

1. Goldman, Joseph L.: Bacteriologic and Clinical Interpretation of the Flora of the Nose and Nasopharynx in Adults, Ann. Otol., Rhin. & Laryng. **59**: 156, 1950.
2. Goldman, Joseph L.: Bacteriologic Aid in Rhinologic Diagnosis and Treatment: Improved Criteria, Laryngoscope **62**: 406, 1952.

CHILDHOOD ECOLOGY SEMINAR

An Experiment in Teaching

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QUITE by accident a short briefing of the new house staff on newborn problems grew into a continuous weekly seminar throughout the year on childhood ecology. It has been so profitable in our hospital that reporting it might help others to integrate the various disciplines, psychiatry, sociology, education, genetics, and so on, that are generally deemed difficult to find time and means of teaching.

The seminar is held after the well-baby clinic on Thursday afternoons from 4 to 5 P.M. In regular attendance are the interns and residents of the pediatric and child guidance services, a psychologist, social workers, nurses, occupational therapists, and others working with or interested in children. The senior staff consists of two or more pediatricians, one or two psychiatrists, and invited guests.

Purposely there is minimal organization in order to permit the exploration of any new phase of child life that may be introduced into the discussion. Some general plan is advisable and ours consists of starting in July with a discussion of the newborn and roughly blocking out the time into the runabout, preschool, and school periods, so that by June the following year the problems of adolescence are taken up, thus growing up with the child during the year.

For practical reasons, our first seminar is on resuscitation and is held in the delivery room, with obstetricians and anesthetists providing the major discussion.

This is followed by a review of questions asked by young mothers regarding their newborn infants. To facilitate this discussion the questions have been typed on blank playing cards and these are shuffled and dealt out to all present, each in turn answering his question or asking for information about it. A number of new questions, as they arise, are added each year. The practicality of having these sessions as soon as feasible after the arrival of the new house staff is obvious. Thereafter everyone more or less speaks the same language to the parents.

The course can then proceed more leisurely and with considerable variation. Rooming-in, breast feeding, mother-child relationships, self-demand are discussed, with members of the obstetrical staff present and participating.

Prenatal education is introduced by the Red Cross nurse who supervises the local courses—the house staff is urged to attend one or more sessions. The visiting nurse explains her plan of home instruction. The role of practical nurses, mothers, and mothers-in-law may come up for comment, and even high school and college courses aimed at educating for parenthood have been discussed.

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The physical growth is not forgotten. There are sessions on the routine examination of the newborn infant, with special discussion by the orthopedists and physiotherapists on congenital hips and clubfeet. Other anomalies are taken up preferably with a geneticist present. The problem of how to tell parents about abnormalities is reviewed. One or more of Gesell's films on growth are shown. Wetzel's Grid and other tables are reviewed. Prematurity, retrolental fibroplasia, and related problems are discussed. One hour is generally devoted to the problem of adoptions.

The first period, roughly of 1 to 3 years, brings up the problems of weaning, walking, talking, self-feeding, training, and the psychological implications of the different methods that are used in helping (or hindering) the child to master these phases of development. This is the negativistic stage of growth in which the child is recognizing his own identity and gaining his first feeling of autonomy.

The next period, roughly 3 to 6 years, is a time in which the child's world expands rapidly. He now begins to formulate ideas of other relationships; he identifies himself with his own sex even though this may be very superficial as was illustrated by one of our children. A boy of 4 years had been hospitalized for circumcision. He objected strenuously to a pair of underpants the nurse brought him, saying they were girls' panties (a common characteristic when identity has first been discovered). The resident then asked him how he knew he was a boy to which he replied, "Can't you see my hair cut?" Not only does he learn his own identity but grandparents, siblings, aunts, and uncles begin to fall into place. He begins to learn something about time and space, facts and fancy, truth and falsehood. It is the age of imaginary playmates, fairies, Santa Claus, and God. He begins to understand that there are living and nonliving things and gains his first, again very simple, concepts of birth and death. It is profitable at this time to have a nursery schoolteacher present at the discussions.

In the next period, namely, school age, the child's environment continues to expand tremendously. He should now be ready to acquire the tools of learning. To date his gain in knowledge has been largely by discovery of relationships and patterns of reaction to life about him. At 6 or thereabouts most children show a readiness to learn to read. This should be followed by a concept of numbers, writing, spelling, etc., a very rich area for further exploration by the combined efforts of pediatricians, psychiatrists, and educators.

This is the age period when the number of outside visitors to the seminar increases. It is well to discuss recreation, religion, the arts, and other extracurricular activities with suitable and interested personnel from these disciplines. It is also timely to discuss agencies and facilities in the community dealing with childhood problems. We have discussed the education of the handicapped, the blind, deaf, retarded, and crippled with special educators in these fields. We have had a dentist and orthodontist join our discussion. Some sessions have been held in other institutions in order to make it more practical; special field trips have been arranged at other times.

The adolescent period is an appropriate time to bring the growth curve up to date and the problems of physical development can be reviewed with films and slides. This is the time to discuss height prediction, obesity, the underweight and endocrine problems in general. There are also good films on the psychology of adolescents. There may be some discussion on delinquency. It is also profitable to discuss with other physicians dermatological and gynecological problems. We have found it worth while to have parents join our discussion, and one year we asked a group of adolescents to our seminar.

The value of this seminar has not only been enthusiastically attested to by members of the house staff now in practice but information has come back to us from members of communities where they have gone praising the pediatrician for his participation and understanding of childhood and community problems.

A number of books have been particularly valuable to us. Deserving special mention are the publications on problems of infancy and childhood, personality development, etc., by the Josiah Macy, Jr., Foundation in New York, Erikson's *Childhood and Society,* and Parkhurst's *Exploring the Child's World.* It is one seminar in which the seniors learn more than the students. Outside participants, dentists, educators, preachers, and recreational workers have expressed enthusiasm for the privilege of participating in the discussions.

HYPOTHYROIDISM IN NEGRO CHILDREN

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IT IS noteworthy that few cases of cretinism among Negroid infants and children have been reported. Until 1936, Gesell[1] was able to discover only three cases of cretinism in the Negro. Bruch and McCune[2] reported twenty-three cases of cretinism in 1944 with no Negro subjects. Numerous reports contain no mention of Negro patients.[3-8] Childs and Gardner[9] also cite the rarity of sporadic cretinism in the Negro in Dr. Lawson Wilkins' clinic in Baltimore.

In view of the rare occurrence of Negro cretins or hypothyroids, three cases are presented.

CASE REPORTS

CASE 1.—H. T., an 11-year-old female patient, first came under our observation because of small stature, slow growth, and poor schoolwork. According to the mother, the child was delivered spontaneously following a normal full-term gestation. She sat alone at 8 months, walked at 2 years, and repeated a few words at about the same time. The patient was the oldest of three children, her two siblings being 8 and 9 years, respectively. Both siblings had normal motor and mental functions.

Physical examination revealed a dull-appearing girl of small stature (she was about the size of a normal 5-year-old child) bearing the following measurements: weight 46½ pounds, height 45½ inches, head circumference 20⅛ inches. Her skin was dry. The pulse rate was 72, blood pressure 85/60. Aside from small stature and decreased activity, there were no other significant physical findings.

The intelligence quotient was 57. X-rays of the wrists revealed only two carpal centers, bone age 2 years 6 months (Fig. 1). Roentgenograms of the pelvis showed generalized decalcification with bilateral epiphyseal dysgenesis of the femoral heads (Fig. 1). Long bone linear measurements: femur, 30 cm.; ulna, 16.5 cm.; tibia, 25 cm. X-ray of the chest presented an enlarged heart with clear peripheral lung fields. There was delayed dentition.

The hemogram and urinalysis were essentially normal. Blood chemistry revealed cholesterol 250, calcium 8.7, phosphorus 6.0 mg. per cent, respectively, alkaline phosphatase 2.9 Bodansky units.

The twenty-four-hour urinary creatinine was 1.75 grams. The basal metabolic rate ranged from minus 11.3 to minus 38.0. Galactose tolerance test was normal. This child never exceeded third grade work despite thyroid therapy at an early age.

CASE 2.—R. D. was admitted to the pediatric service at the age of 10 years with a history of retarded mental and physical development. She was lethargic and about the size of a 5- or 6-year-old child. She responded very slowly to questioning. Her facies was dull with thickened features. She was moderately obese with dry scant hair and extremely dry skin. The six-year molars and lower permanent central incisors were erupted. However, there was a high grade malocclusion and some dental hypoplasia.

The patient was small for her age (Fig. 2). Measurements were:

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weight 57 pounds, height 43 inches, head circumference 21 inches, pulse 74, blood pressure 80/60. There were no other unusual physical findings except shortened fingers.

Roentgenograms revealed a bone age of 5½ years (Fig. 3). Epiphyseal dysgenesis of both femoral heads was marked (Fig. 3). Thyroid medication was instituted but follow-up was limited.

Fig. 1.—Case 1. Three epiphyseal centers appear at wrists (capitate, hamate, and distal epiphysis of radius). Bone age 2 years 6 months. Epiphysis of first metacarpal is faintly visible. Note epiphyseal dysgenesis of both femoral heads, more marked on the right.

The hemogram and urinalysis were normal. Cholesterol was 290, calcium 12.6, phosphorus 3.2 mg. per cent, respectively. The alkaline phosphatase was 7 Bodansky units. Serological tests for syphilis were negative. Basal metabolic rate ranged from minus 15.1 to minus 27.5.

Case 3.—T. B. was first seen at the age of 26 months when his weight was 21½ pounds and height 26½ inches. The baby was apparently normal at birth. At 7 months the mother noticed weakness of the neck muscles and slow activity. The first teeth erupted at 10 months of age.

At 26 months the infant crawled but did not walk. He had a poor appetite and was chronically constipated.

The mother had seven previous pregnancies, four of which resulted in miscarriages. There were no prenatal or natal difficulties associated with this child.

A physical examination of the child exhibited flabby musculature and poor mentality with sluggish reflexes. The skin was dry with brittle hair. The facies was dull with a large protruding tongue. An umbilical hernia was present (Fig. 4). His stature was dwarfed. Roentgenograms made at the age of 26 months showed no

Fig. 2.—Case 2. Front view shows dwarfed stature, dull facies, and protruding abdomen more apparent from lateral view.

Fig. 3.—Case 2. Roentgenogram of pelvis reveals marked bilateral epiphyseal dysgenesis. Note flattened and fragmented appearance of femoral epiphyses. Capitate, hamate, triquetral, lunate, navicular, greater and lesser multangular centers are present at the wrists, as well as metacarpal and phalangeal epiphyses. Bone age 5 years 6 months.

ossification centers at the wrist and only four at the ankle (Fig. 5).

COMMENT

Sporadic cretinism results from complete or partial failure of a functioning thyroid gland during intrauterine life. The rudimentary or absent thyroid gland probably represents an embryonic defect. Although the condition is congenital, recognition may be delayed for some time.

Fig. 4.—Case 3. Note typical cretinoid facies, protruding abdomen and umbilical hernia.

The hypothyroidism in all three of our cases was probably prenatal in origin. Although Cases 1 and 2 did not come under observation until after the age of 10 years, the presence of extensive dysgenesis involving the femoral heads indicated that thyroid deficiency began before the twelfth month of life. The dwarfism and severe mental retardation also pointed to the onset of hormonal deprivation very early in life.

All three of the children presented mental and physical retardation as well as other signs of thyroid deficiency. Case 3 exhibited the classical picture of florid cretinism in a very young child. The two older children (Cases 1 and 2) presented dwarfism, mental torpor, and epiphyseal dysgenesis as outstanding findings. In Case 1 the osseous dysgenesis was of considerable diagnostic importance because the hypothyroidism was somewhat masked, and on gross physical inspection the child appeared relatively normal except for her small stature. Wilkins[10] has emphasized the importance of epiphyseal dysgenesis in the diagnosis of hypothyroidism. He has not seen this specific osseous lesion in any type of dwarfism other than that occurring in hypothyroidism. Other characteristic but less specific roentgenologic findings involving the osseous system in this disease are delay in appearance of ossification centers and marked decrease in linear growth and calcification of the diaphysis.

Cardiac enlargement was present in Case 1. Boratz and Bronstein[11] postulate three possible mechanisms for cardiac enlargement in cretinism: (1) interstitial edema; (2) anemia; and (3) infiltration of heart muscle by mucinlike material.

The three children reported here all showed evidence of mental retardation. This characteristic feature of

congenital thyroid deficiency has been attributed by Wilkins[12] to the following mechanism: (1) slowing of mental reactivity and responsiveness, (2) retardation of development of the brain, (3) irreparable damage to brain cell in some cases, and (4) congenital malformation of the brain. It is possible that the latter two conditions may explain the mental deficiency of adequately treated cretins. Electroencephalographic studies tend to substantiate this observation. If made in early infancy, electroencephalographic readings may be of prognostic importance with distinct cerebral dysfunction being indicative of poor results to thyroid therapy.

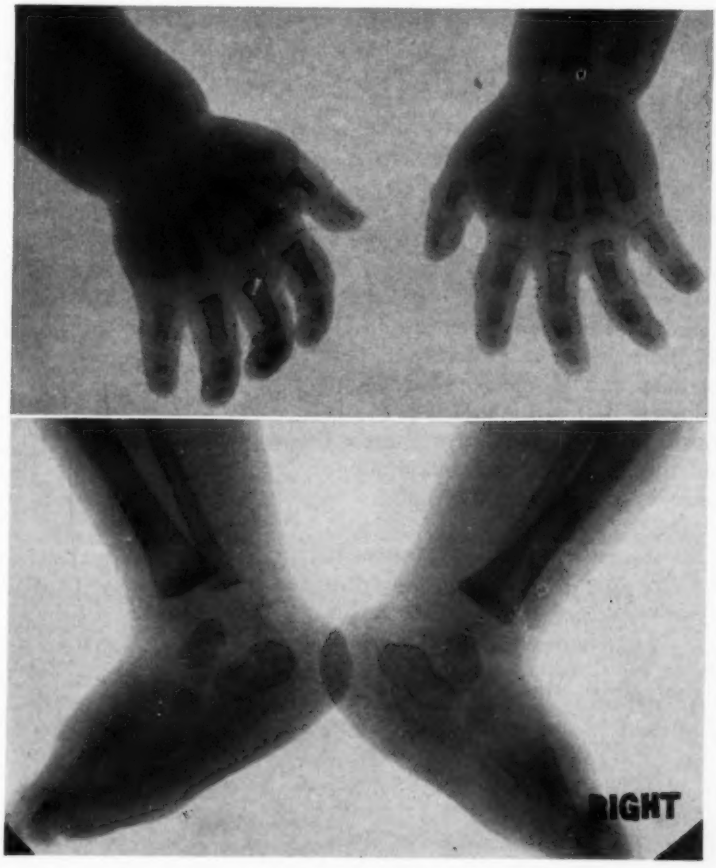

Fig. 5.—Case 3. Roentgenograms of ankles reveal only four tarsal centers (talus, calcaneus, cuboid, and external cuneiform). There are no carpal centers present at wrist. This case presents marked retardation of osseous development.

The three cases presented here were observed many years ago before protein-bound iodine determinations became available for clinical use. All of the patients received thyroid medication but unfortunately

the results were not very satisfactory because of the parents' delay in seeking early and continuous medical care for the children.

Wilkins recommends initial doses of ¼ to ½ grain of desiccated thyroid (U.S.P.) daily gradually increased to a maintenance dosage of 1 to 2 grains daily for infants and 2 to 3 grains for children over 3 years of age. The dose for the individual child, however, should be adjusted to the optimum physiological response desired rather than arbitrarily giving a stereotyped amount on the mere basis of age and weight.

SUMMARY

Three cases of hypothyroidism in Negro children are reported. Our observations and the paucity of reported cases in Negro subjects indicate that sporadic cretinism or hypothyroidism is quite rare in children of this racial group.

The clinical data in Case 3 was supplied by Dr. Alonzo deG. Smith, Clinical Professor of Pediatrics, Howard University.

REFERENCES

1. Gesell, Arnold: Clinical Mongolism in Colored Races: With Report of a Case of Negro Mongolism, J. A. M. A. **106:** 1146, 1936.
2. Bruch, Hilda, and McCune, Donovan J.: Mental Development of Congenitally Hypothyroid Children, Am. J. Dis. Child. **67:** 205, 1944.
3. Radwin, Leo S., Michelson, J. P., Berman, Abraham B., and Kramer, B.: End Results of Treatment of Congenital Hypothyroidism: Follow-up Study of Physical, Mental and Behavioral Development, Am. J. Dis. Child. **78:** 821, 1949.
4. Stanbury, John B., and Hedge, Alice N.: A Study of a Family of Goitrous Cretins, J. Clin. Endocrinol. **10:** 1471, 1950.
5. Granbemeyer, W. H.: Cretinism and Mongolism in the Same Family, J. PEDIAT. **36:** 656, 1950.
6. Collier, W. T.: Cretinism and Mongolism in the Same Family, Brit. M. J. **2:** 1044, 1930.
7. Bronstein, J. P., Bower, L. E., and Murphy, J.: Familial Cretinism, Am. J. M. Sc. **205:** 114, 1943.
8. Gill, Morton A.: Bronchopneumonia in a Cretin Before and After Treatment With Thyroid, Am. J. Dis. Child. **15:** 199, 1940.
9. Childs, Barton, and Gardner, L. I.: Etiologic Factors in Sporadic Cretinism: An Analysis of 90 Cases From Abstracts of Society for Pediatric Research, Atlantic City, May 4-6, 1953.
10. Wilkins, L.: Epiphyseal Dysgenesis Associated With Hypothyroidism, Am. J. Dis. Child. **61:** 13, 1941.
11. Boratz, J. J., and Bronstein, P.: The Heart in Children With Thyroid Deficiency, Am. J. Dis. Child. **64:** 71, 1942.
12. Wilkins, L.: The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence, Springfield, 1950, Charles C Thomas, chap. V (Hypothyroidism).

MONILIA ONYCHIA

Report of a Case in a 51-Day-Old Premature Infant

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THRUSH, a fungus infection of the mucous membranes, is universally recognized as a common disease of infancy, and is frequently regarded as benign. Ludham and Henderson[1] in 1942 observed a greater incidence of thrush in premature infants when compared with full-term infants and were further able to correlate the longer duration of hospital stay with an increased incidence of the infection, the premature infants showing a corespondingly greater increase in incidence. Bottle-fed children were observed to have a greater incidence than breast-fed children.

Although Ludham and Henderson were unable to show any correlation between maternal vaginal infection caused by Monilia and thrush in the newborn infant, Woodruff and Hesseltine[2] in 1938 expressed the opinion that the incidence of oral thrush in the newborn showed a definite relationship to the presence of the fungus in the generative tract of the mother. In 1940 Hesseltine[3] recommended a single prophylactic application of a 1 per cent aqueous solution of gentian violet immediately after birth to the oral cavity of any infant whose mother had vaginal mycosis. Anderson and associates[4] in 1944 observed that oral thrush appeared earlier and more frequently in infants whose mothers had vaginal moniliasis. It is possible, too, that the monilial infection is transferred to the infant through contaminated objects rather than from the birth canal at the time of birth.

Although *Candida albicans* regularly emerges in abundance in the oral cavity and gastrointestinal tract of patients receiving wide-spectrum antibiotics, Kligman[5] in 1952 stated: "The wide-spectrum antibiotics were not found to enhance the growth of *C. albicans* in vitro nor to potentiate mycotic disease in animals with experimental moniliasis." Various theories have been advanced to explain the complication of moniliasis associated with antibiotic therapy, ranging from freedom from competition with bacteria for nutrition to a complex metabolic interrelationship dependent upon the reduced amount of vitamin B complex.

Thrush is common in the newborn period and other manifestations of moniliasis are reported with increasing frequency in the pediatric literature. However, Monilia onychia is an unusual lesion in the younger age groups.[6] The youngest reported case of Monilia onychia is believed to be that of Riley[7] who described typical Monilia onychia in a 4-year-old child. The child had apparently acquired the lesion of the thumbnail as a result of sucking his thumb at a time when he had Monilia infection of the oral cavity.

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CASE REPORT

J. S. H., a white female premature infant weighing 1,490 grams, was transferred immediately after birth in another hospital to the Jefferson Davis Hospital Premature Unit. On admission the infant appeared to be in good condition. Five hours after admission a fine coalescent papular erythematous rash over the back and abdomen was noted for the first time. No definitive dermatologic diagnosis was made. The rash continued to spread and on the third day vesicular pustular lesions were noted on the scalp. The infant received penicillin (75,000 units per twenty-four hours) and Gantrisin (0.12 Gm. per kilogram per day) for three days without evident improvement of the skin lesions. At that time the body temperature dropped to 92° F., and the infant appeared listless. The possibility of a septicemia was then considered. Treatment was changed to Aureomycin (25 mg. per kilogram of body weight per day). The skin lesions and general symptoms cleared rapidly. Aureomycin was continued over a seven-day period (seventh to fourteenth day of life).

Fig. 1.—Monilia onychia. Ridged, laminated, friable appearance of fingernails and toenails at 2 months of age.

On the sixth day of life whitish adherent plaques were noted on the mucosa of the lips and tongue. The diagnosis of thrush was made and the lesions were treated topically with a 1 per cent aqueous solution of gentian violet. After four days of treatment the rash disappeared and the local applications were discontinued.

The course in the hospital following the end of the second week was un-

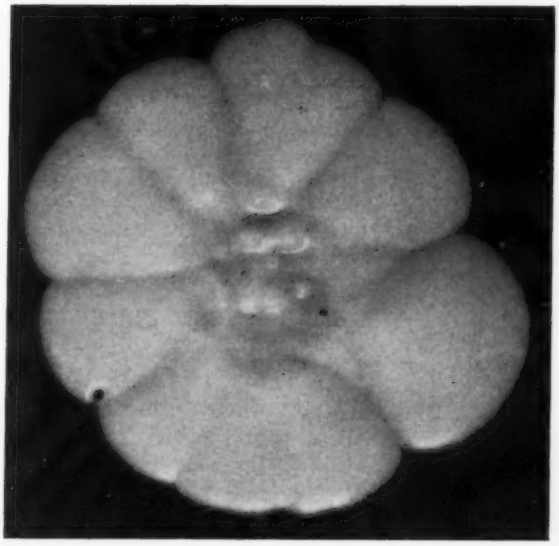

Fig. 2.—Typical colony of Monilia grown from nail scrapings inoculated into Sabouraud's media.

Fig. 3.—Appearance of fingernails and toenails at 5 months of age. No treatment was given.

eventful except for crusting and scaling of the skin of the scalp, particularly in the postauricular region. The infant regained birth weight, and the body temperature became stabilized by the seventeenth day of life.

On the fifty-first day of life, it was noted that the patient had laminated, ridged, friable, brownish yellow onychia of several of the fingernails and the toenails (Fig. 1). The gross appearance was that of a fungus infection of the distal parts of the nails involved. A definite line of demarcation from normal nail was present. At this time the physical examination was otherwise negative. The nails were first cleansed thoroughly with alcohol and then scraped with a sterile scalpel blade and the scrapings caught in several sterile test tubes. Pseudomycelia were seen in hydroxide preparations made from the nail scrapings.

Cultures on Sabouraud's media were positive for Monilia and when transferred to cornmeal media, Monilia was readily grown. Stool cultures for Monilia were negative.

Two weeks after the lesions had been first observed, the lines of demarcation were noted distal to the original sites. At 67 days of age the lesions had virtually cleared. The patient was not seen again until 5 months of age at which time the lesions had completely cleared (Fig. 3). No treatment for the Monilia onychia had been given.

Past history revealed that the mother, during pregnancy, had had a rather severe vaginitis which the attending physician had thought to be a "mixed type" of infection. The infection failed to respond to sitz baths, douches, and Aureomycin inserts, but had responded fairly well to Floraquin suppositories. Vaginal pruritus had continued until after the delivery. Vaginal culture taken from the mother two months post partum had been reported to be negative for Monilia.

Fig. 1 demonstrates the appearance of the involved nails; Fig. 2 shows a typical colony on a culture plate inoculated with scrapings from the nails; Fig. 3 shows the normal appearance of the nails when the patient was 5 months of age.

SUMMARY

1. Monilia onychia, hitherto unreported in infants, is reported in a 51-day-old premature infant.

2. The mother of this patient had a vaginitis during pregnancy which cleared after delivery. No cultures were obtained.

3. The patient received penicillin, Aureomycin, and Gantrisin during her stay in the Premature Unit. Clinical thrush was present in the oral cavity forty-five days prior to the time when the onychia were first noted.

4. With growth of the nails, the lesions had virtually disappeared by the time the infant was discharged at 67 days of age. The nails appeared normal when the patient was again seen at 5 months of age. The patient received no treatment for the Monilia onychia.

REFERENCES

1. Ludham, G. B., and Henderson, J. L.: Neonatal Thrush in a Maternity Hospital, Lancet **242**: 64, 1942.
2. Woodruff, P. W., and Hesseltine, H. C.: Relationship of Oral Thrush to Vaginal Mycosis and the Incidence of Each, Am. J. Obst. & Gynec. **36**: 467, 1938.
3. Hesseltine, H. C.: Vulval and Vaginal Mycosis and Trichomoniasis, Am. J. Obst. & Gynec. **40**: 641, 1940.
4. Anderson, N. A., Sage, D. N., and Spaulding, E. H.: Oral Moniliasis in Newborn Infants, Am. J. Dis. Child. **67**: 450, 1944.
5. Kligman, A. M.: Are Fungous Infections Increasing as a Result of Antibiotic Therapy? J. A. M. A. **149**: 979, 1952.
6. Haley, L. D.: Mycotic Diseases in Pediatric Practice, J. PEDIAT. **41**: 104, 1952.
7. Riley, K. A.: Monilial Infection of the Thumb Nail, Arch. Dermat. & Syph. **59**: 589, 1949.

Medical Progress

INTESTINAL OBSTRUCTION IN THE NEWBORN INFANT

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IN RECENT years great progress has been made in the treatment of intestinal obstruction in the newborn infant, and an encouraging number of successful surgical results have been reported. However, it is difficult to assess the problem of obstruction in the newborn infant by perusal of the literature since most of the articles are limited to a specific lesion and most of the larger series include cases beyond the newborn period.

In reviewing our own experience, we have chosen for study only those cases of intestinal obstruction occurring from birth to 30 days of age, since this is the period which is generally referred to as "newborn" by pediatricians and public health officers. Our material includes 134 consecutive cases of intestinal obstruction in the newborn infant seen at the Babies Hospital (New York) between the years 1939 and 1952. In each case the diagnosis was confirmed at operation or at autopsy. The study does not include obstructive lesions of the esophagus, stomach, or rectum. The rectal anomalies have been recently reported.[31]

ETIOLOGY

A useful outline of the etiology of intestinal obstruction in the newborn infant and in the older child is presented in Table I. The causes of obstruction in the present series, as well as their frequency and results, are listed in Table II.

CLINICAL FINDINGS

There were eighty-six males and forty-eight females in this group.

Vomiting was the earliest and most constant symptom. The onset, type, and severity of vomiting depended on the specific cause of the obstruction. At first the vomitus was always bile stained unless the obstruction occurred above the ampulla of Vater. In duodenal obstructions it was often brilliant green and sometimes forceful. Later, in the lower obstructions, the vomitus was malodorous, fecal in character, or it resembled meconium.

In complete obstructions no stool was passed or there was the passage of a small stool which resembled meconium but was mucoid and gray. In the incomplete obstructions the stools were sometimes normal. Abdominal distention was minimal and confined to the upper abdomen in cases of high obstruction. It was usually more severe and progressive in the lower obstructions, and marked distention was seen when paralytic ileus developed.

Gastric peristaltic waves were seen in some cases of duodenal obstruction, and intestinal peristalsis was observed in a few of the lower obstructions. As in the adult, auscultation of the abdo-

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men revealed hyperperistalsis with high-pitched intestinal sounds, but the abdomen was "silent" when paralytic ileus supervened.

Tenderness and rigidity were difficult signs to appraise in the newborn infant, particularly in the premature group. When gangrene or eral circulatory collapse was found. However, many of the cases of complete obstruction, even of the closed-loop variety with impairment of the circulation, showed minimal or no signs of peritoneal irritation.

The temperature was usually normal or only slightly elevated but rose

TABLE I. CAUSES OF INTESTINAL OBSTRUCTION IN THE NEWBORN INFANT

I. *Mechanical*
- A. Congenital
  - 1. Intrinsic
    - a. Atresia and stenosis
    - b. Meconium ileus
    - c. Hypertrophic pyloric stenosis
  - 2. Extrinsic
    - a. Malrotation with or without mid-gut volvulus
    - b. Volvulus without malrotation (localized)
    - c. Congenital peritoneal bands
    - d. Incarcerated hernia—inguinal, diaphragmatic, internal
    - e. Annular pancreas
- B. Acquired
  - 1. Intussusception
  - 2. Peritoneal adhesions
    - Previous surgery
    - Previous infection

II. *Neurogenic*
- A. Defective intrinsic innervation (congenital)
  - 1. Colon and rectum—congenital megacolon
  - 2. Small intestine
- B. Paralytic ileus
  - 1. Cerebral injury
  - 2. Infection

TABLE II. INTESTINAL OBSTRUCTION IN THE NEWBORN INFANT (BABIES HOSPITAL 1939-1952)

CAUSE	NO. OF CASES	RECOVERED	DIED	MORTALITY (%)
Atresia and stenosis	46	19	27	58.7
Meconium ileus	20	7	13	65
Malrotation	20	16	4	20
Neurogenic (congenital)	14	11	3	21.4
Congenital peritoneal bands	8	6	2	
Localized volvulus	5	1	4	
Meconium peritonitis (cause undetermined)	5	1	4	
Inguinal hernia	5	5	0	
Internal hernia	2	1	1	
Intussusception	3	1	2	
Annular pancreas	1	1	0	
Adhesions, postoperative	2	2	0	
Multiple causes	3	3	0	
Total number of cases	134	74	60	44.8

perforation of the intestine occurred, the characteristic picture of extreme distention, boardlike abdominal spasm, labored respirations, especially with expiratory grunt, and signs of periph- rapidly to high levels in the presence of dehydration or peritonitis. However, the temperature was often normal even in the presence of gangrene and peritonitis, especially in the pre-

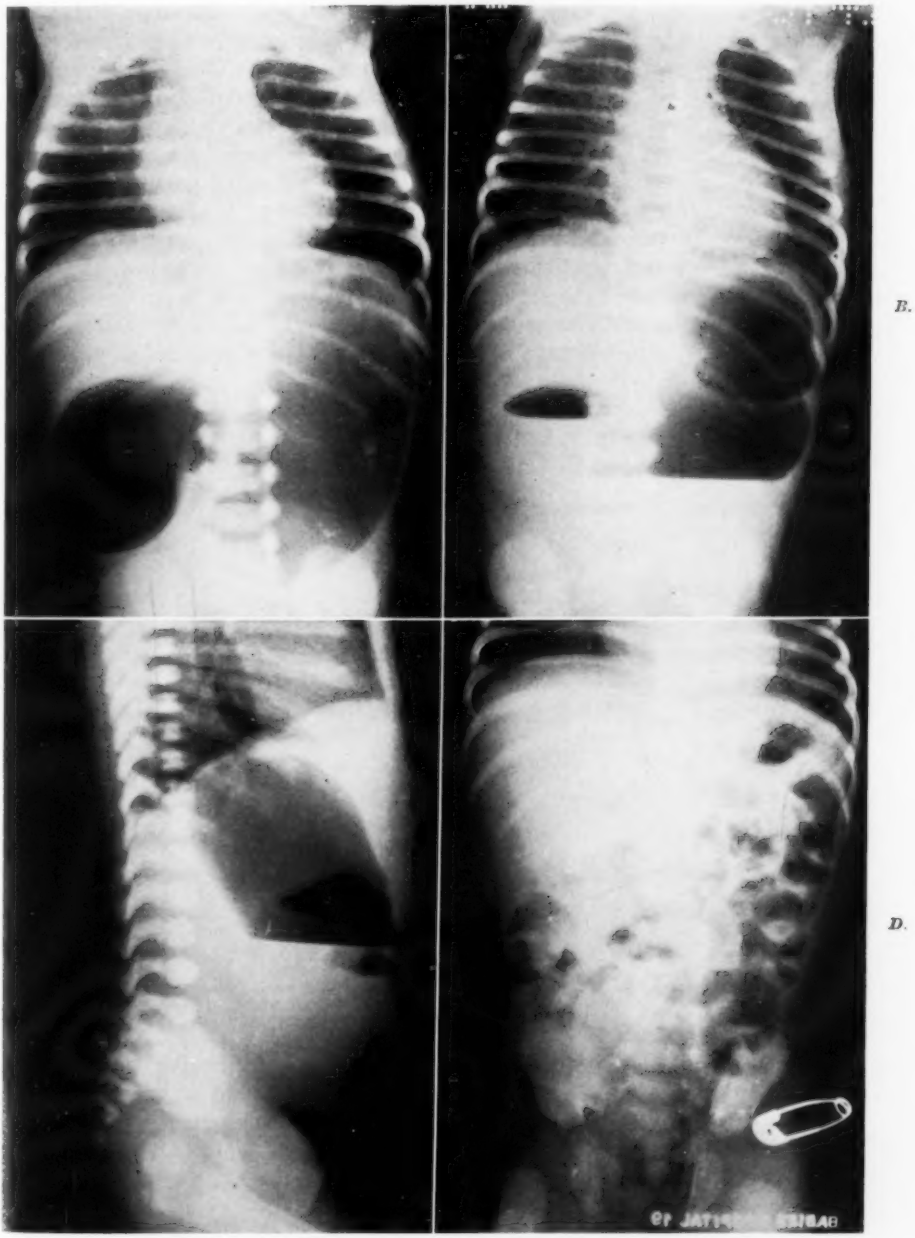

Fig. 1.—Atresia of the third portion of the duodenum. Three-position plain roentgenograms show dilatation of stomach and upper duodenum with fluid levels. Contrast medium not necessary for diagnosis. *A*, Supine anteroposterior view. *B*, Erect anteroposterior view. *C*, Lateral erect view. *D*, Ten days after duodenojejunostomy, showing normal distribution of gas.

mature infant. Sudden drop in temperature to a subnormal level, or a sustained subnormal temperature was usually ominous.

As indicated by Moore[25] there is no essential difference in the physiologic disturbances of acute intestinal obstruction occurring in the infant and in the adult. In this newborn group, dehydration, electrolyte imbalance, and "toxemia" assumed the same significance as in the adult except that the disturbances were relatively more acute and often fulminating. As expected, the changes were more severe when the obstruction was high and when there was gangrene of the bowel.

Fig. 2.—Jejunal obstruction due to atresia, showing distended upper small intestine with fluid levels. Contrast medium not necessary for diagnosis.

The hemoglobin and red blood count were nearly always elevated because of hemoconcentration. The white blood count was usually elevated but it was often normal or depressed even in the presence of gangrene and peritonitis. Chemical examination of the blood was not done preoperatively in every case but a study of the available laboratory data revealed the following: elevation of the nonprotein nitrogen, decrease of plasma sodium, chloride, and potassium levels, and reduction of the carbon-dioxide combining power more commonly than alkalosis.

Microscopic examination of the meconium (Farber test) was sometimes helpful. The absence of cornified epithelium ingested with the amniotic fluid by the fetus is diagnostic of atresia.[10] It should be emphasized that this test is of practical significance

Fig. 3.—Low ileal obstruction due to meconium ileus. Contrast medium not necessary for diagnosis of intestinal obstruction.

only in cases of atresia. Care should be taken to obtain a sample of the center of the meconium for the examination so that epithelial cells of the anal canal or of the perineum are not included in the specimen. We have found this test a helpful adjunct on some occasions but have not used it routinely.

Roentgen examination was, of course, the most important single diagnostic measure employed and the findings were usually characteristic. Ladd and Gross,[20] Donovan,[7] Silverman and Caffey,[32] and others have emphasized the importance of the plain roentgenogram of the abdomen without contrast media. In almost all of the cases this furnished the desired information. With the conventional three-position views, the distribution of air in the intestine was usually diagnostic and often located the approximate level of obstruction (Figs. 1, 2, 3). The oral administration of barium in the usual case of intestinal obstruction in the newborn infant is not necessary and it can even be dangerous. The material may be aspirated or it may become inspissated in the intestine postoperatively and cause obstruction at the anastomosis or in the distal collapsed bowel. Barium has also been found free in the peritoneal cavity, probably having contributed to the perforation of gangrenous bowel. We have also had the unfortunate experience of trying to remove it from the intestine during the performance of a difficult anastomosis. Occasionally, in cases of intermittent, incomplete obstruction, the use of a contrast medium was considered necessary. In these instances, colloidal barium or, less frequently, Lipiodol was used. The barium enema was helpful by demonstrating malposition of the colon in malrotation (Fig. 6) and it was also useful in distinguishing small intestine from colon in some cases.

ATRESIA AND STENOSIS

Atresia and stenosis were the most common causes. Atresia was found about twice as commonly as stenosis. Together they comprised 34.3 per cent of the group (Table II).

Although the differentiation between atresia and stenosis was usually apparent, it was not always possible to clearly distinguish the two lesions clinically. The distinction was sometimes difficult even in the operating room and the final diagnosis had to be made in the pathologic laboratory or at autopsy.

Embryologically, atresia represents a failure of recanalization of the intestinal canal during the end of the second month of fetal life, resulting in a diaphragm completely occluding the lumen or in a blind sac which may or may not be connected with the distal intestine by a fibrous band. Stenosis results from partial recanalization, giving rise to an incomplete diaphragm or to a narrowing of the intestinal lumen.[20]

Review of the literature on this subject is confusing since the terms "atresia" and "stenosis" are often used indiscriminately. For the purposes of standardization in future recording, Evans[9] has recently proposed the terms "total or complete atresia" and "subtotal or partial atresia" (stenosis). Glover and Barry[14] did not attempt to separate atresia from stenosis in their series, stating: "The classification is difficult at best, and the only functional difference between the two is in the relative degree of obstruction produced." Gross[15] distinguishes the lesions in his large group of cases and we have always found the division useful.

The distribution of the lesions is shown in Table III. The ileum and duodenum were the most common sites of atresia. Ileal atresias were usually seen in the distal third of the ileum.

TABLE III. ATRESIA AND STENOSIS

SITE AND NO.		RECOVERIES	DEATHS	
Atresia				
Duodenum	11	5	6	
Jejunum	5	1	4	
Ileum	13	4	9	
Jejunum and ileum	1	0	1	
Colon	1	1	0	
Total	31	11	20	(65%)
Stenosis				
Duodenum	7	5	2	
Jejunum	2	0	2	
Ileum	4	2	2	
Colon	2	1	1	
Total	15	8	7	(47%)
Total number of atresia and stenosis	46	19	27	(58.7%)

of atresia. In one of these, there were no fewer than twelve points of atresia (Fig. 4). The incidence of multiple atresias is reported as high as 15 per cent.[6] None of the fifteen cases of congenital stenosis in this series showed more than one point of obstruction and the author was unable to find any report of multiple stenosis in the literature. We have, however, recently seen a case of multiple congenital stenosis in an older child. Atresia was seen in two forms: In seven cases the intestine ended as a blind pouch which was not connected with the distal bowel. In

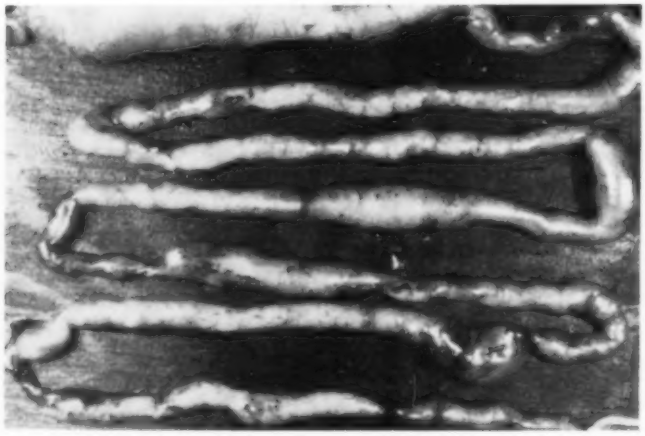

Fig. 4.—Multiple atresias of jejunum and ileum.

Duodenal atresias usually occurred in the third and fourth portions; only one was found in the second part of the duodenum above the ampulla. Stenosis was seen most often in the duodenum, each instance in the third or fourth portion. It should be emphasized that congenital atresia and stenosis of the colon, exclusive of the rectum, are quite rare.

More than one site of atresia was found in three of the thirty-one cases the other twenty-four cases the intestine was grossly continuous and the obstruction was due to a diaphragm completely occluding the lumen. Gangrene and perforation of the proximal bowel with meconium peritonitis was found in four of the thirty-one cases of atresia and in two of the fifteen cases of stenosis before operation.

The results for this group are shown in Table III. In four of the forty-six cases death occurred before any opera-

tion was performed. Although the series is too small to permit any broad generalizations, the following observations can be recorded:

(1) The establishment of a primary anastomosis in lesions of the small intestine is preferable in all cases. Enterostomy, as a definitive procedure, should be avoided. Infants do not tolerate the loss of small intestinal contents for a prolonged period in spite of vigorous parenteral replacement. Although some success has been reported with enterostomy in isolated cases, we have used it in only three cases as a preliminary procedure and have followed it by an anastomosis in a short time. This limited experience would lead us to avoid primary enterostomy except in the most unusual circumstances. Colostomy is usually better tolerated and can be used as a definitive procedure when necessary.

(2) All other factors being equal, delay in diagnosis directly affects the prognosis. Apart from the obvious complications of gangrene, dehydration, and electrolyte imbalance, delay in diagnosis directly increases the complexity of the operation. The disproportion between the dilated proximal bowel and the small distal bowel increases as the distention progresses. This can create serious technical difficulties in the performance of an anastomosis which is difficult even under the best of conditions.

(3) The "open" type of anastomosis was employed in all cases. It was usually made in two layers according to the technique described by Ladd and Gross.[20] In the more difficult cases with a very small distal intestine I prefer a single-layer anastomosis using interrupted 00000 arterial type of silk.

(4) Saline should always be instilled into the distal bowel in order to increase the diameter of the lumen and to ascertain the presence of other obstructions.

(5) A side-to-side type of anatomosis was done most often and was considered the safest. The bowel was usually not divided nor was any segment resected unless it was gangrenous or perforated. The end-to-end type of anastomosis should be avoided. However, in some cases of marked disparity in the size of the loops which were to be joined, the end-to-side type of anastomosis (using the end of the distal loop and the side of the proximal loop) seemed more suitable and was successfully employed.

(6) Postoperative decompression of the intestine in order to protect the suture line from continued distention of the proximal bowel was important. This was best achieved by a small catheter or a small Miller-Abbott tube which the surgeon directly manipulated through the pylorus and down the intestine to within one or two feet of the anastomosis. Although helpful, ordinary nasogastric suction did not always give the desired decompression of the small intestine. In two cases this decompression was assured by performing a complementary tube enterostomy just proximal to the anastomosis.

(7) In this small series of duodenal obstructions, the retrocolic duodenojejunostomy gave better results than gastrojejunostomy.

(8) In general, the patients with congenital stenosis fared better than did those with atresia, and the duodenal obstructions had a better prognosis than the ileal (Table III).

Twenty of the thirty-one patients with atresia died. Surgery was performed in all but three of the cases. The causes of death will be discussed later. Eleven patients survived and have been carefully followed. Ten of these patients have excellent results to the present writing. The follow-up periods have been: 1 for six months, 2 for one year, 2 for two years, 2 for three years, 1 for four years, and 2 for six years. One patient still has a colostomy. This was required for a malfunctioning colocolostomy which had been performed for atresia of the colon. Subsequently, another anastomosis was done which is functioning well, and he is awaiting closure of the colostomy.

four years, 2 for six years. One patient recently had a transverse colostomy done for stenosis of the sigmoid colon and is awaiting further definitive surgery.

MECONIUM ILEUS

Some cases of cystic fibrosis of the pancreas are associated with intestinal obstruction in the immediate newborn period. The relation of these two conditions has been established by the work of Farber[11] and of Andersen,[1, 2, 3] who have shown that the ileus is based on the absence or marked diminution of pancreatic enzymes, especially trypsin. This lack of pancreatic digestion results in an abnormal meconium which

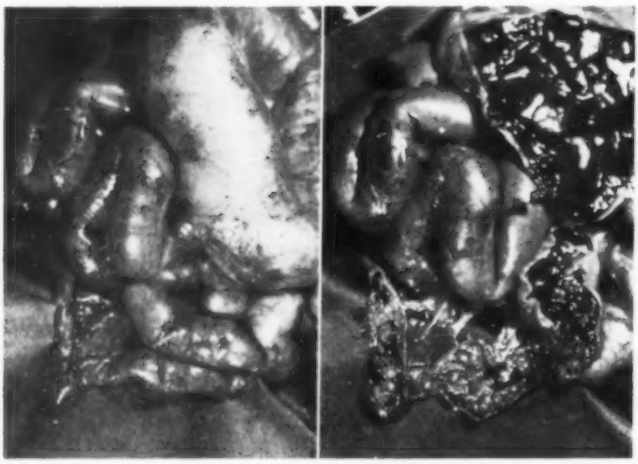

Fig. 5.—Meconium ileus. Note dilatation and hypertrophy of upper ileum and characteristic small colon. The upper ileum contains tenacious, viscid neconium. The terminal ileum contains dry, gray meconium.

All but one of the group of fifteen patients with congenital stenosis came to surgery. Seven of the cases were fatal. Seven of the eight survivals have had good results. The follow-up periods have been: 1 for six months, 1 for one year, 2 for two years, 1 for

is sticky, viseid, and mucilaginous. It becomes inspissated in the lower ileum and blocks the intestinal canal. The efforts of the ileum to propel this abnormal material result in hypertrophy of its walls long before birth of the child.

Characteristically, there is hypertrophy and dilatation of the mid-ileum which contains semifilled and tenacious meconium. The distal 10 to 20 cm. of ileum are filled with hard, gray concretions resembling dry putty. The large intestine is usually empty, small, and hypoplastic (Fig. 5).

These patients commonly show severe distention and there is a hard consistency to the abdomen. If seen very early, the abdomen may be soft, and one may palpate rubbery loops of intestine which pit on pressure. Rectal examination often reveals an unusually small anus and rectum. Although I have made this observation in some cases of atresia of the small intestine, it has been more impressive in cases of meconium ileus. The most important diagnostic feature is a familial history of the disease or of pancreatic cystic fibrosis. Some cases show roentgen evidence of gas bubbles in the distal small bowel and Pugh[30] states that Neuhauser was able to make the diagnosis in four out of ten cases by this finding.

In 1942 Hurwitt and Arnheim[19] reviewed the literature and were unable to find any instances of recovery. In 1948 Hiatt and Wilson[16] described a new method of treatment and reported the first successfully treated cases. Five of their eight patients were relieved of intestinal obstruction, and they are all included in the present series.

Our series includes twenty cases of meconium ileus with seven recoveries (Table IV). It should be noted that fourteen of these patients had associated lesions which could lead the surgeon to an erroneous diagnosis unless he recognizes the basic pathology of the disease. In ten cases, volvulus of the hypertrophied segment of ileum had occurred; four with gangrene. There were associated congenital peritoneal bands in three patients and malrotation with volvulus of the midgut in one. All of the patients had cystic fibrosis of the pancreas. The diagnosis was either established at autopsy or it was confirmed in the early postoperative period by a study of the duodenal secretions. Patients with fibrocystic disease of the pancreas had a trypsin concentration of less than 10 viscosimetric units per cubic centimeter of duodenal juice.

TABLE IV. MECONIUM ILEUS

Number of cases		20
Associated pathology	14	
Volvulus of hypertrophied segment (four with gangrene)	10	
Congenital peritoneal bands	3	
Malrotation	1	
Deaths	13	(65%)

Treatment consists of ileotomy with removal of the meconium as described by Hiatt and Wilson.[16] Pancreatin, 0.5 Gm. dissolved in 10 to 15 c.c. of normal saline, is always given through a nasogastric tube at six-hour intervals, starting on the second postoperative day. The digestive agent is no longer instilled into the ileotomy at the time of operation because of the danger of local digestion at the suture line.

The regimen advocated by Andersen[3] is instituted as soon as possible. These patients are given a low fat, high protein diet. They require a high vitamin intake, particularly vitamins A, B complex, C, and D. All respiratory infections are vigorously treated at their onset with appropriate antibiotics and sulfonamides.

Surgery was performed in all twenty cases of meconium ileus. Thirteen patients died. In eight of these, the

diagnosis was not suspected and treatment was directed to reduction or resection of coexisting volvulus or to division of congenital peritoneal bands thought to be the cause of obstruction. In one case the disease was recognized but nothing could be done because of associated malrotation with volvulus and gangrene of the entire midgut segment. In the remaining four fatalities the disease was recognized and treated in accordance with our present ideas but the patients succumbed in the early postoperative period.

Seven patients recovered from operation. Ileotomy with removal of the meconium from the bowel was performed in all of these cases. In addition, one patient had resection of a gangrenous volvulus with anastomosis, and two patients had reduction of an associated volvulus. The fate of these seven patients is summarized:

Case 1: Readmitted to hospital because of severe laryngo-tracheobronchitis eight weeks after operation. Tracheotomy was done but the patient died.

Case 2: Frequent respiratory infections. Died three years postoperatively of bronchiectasis and multiple lung abscesses.

Case 3: Living three months after operation. Asymptomatic.

Case 4: Living eighteen months postoperatively. Frequent but mild upper respiratory infections.

Case 5: Living twenty-eight months postoperatively. Bronchopneumonia at age of 2 years required admission to the hospital.

Case 6: Living five and a quarter years postoperatively. Occasional mild respiratory infection.

Case 7: Living seven and a quarter years postoperatively. Frequent bouts of bronchopneumonia.

MALROTATION

Knowledge of the normal process of intestinal rotation is essential for the proper understanding of these anomalies. Since adequate consideration of the embryology is beyond the scope of this paper, the reader is referred to the textbooks of Patten[28] and of Ladd and Gross.[20] Excellent descriptions of the errors of rotation have been presented by McIntosh and Donovan[23] and by Gardner and Hart.[13]

In this group of 134 cases of intestinal obstruction in the newborn infant only twenty were due to malrotation. Although many other cases were seen after this thirty-day period, they are not included in this study.

Anomalies of rotation gave rise to intestinal obstruction in two ways in this small series.

(1) Most commonly the obstruction was based on volvulus of the midgut loop. This portion of intestine includes the jejunum, ileum, and large intestine up to the middle of the transverse colon, i.e., the segment supplied by the superior mesenteric artery. Failure of fixation of the mesentery, the short primitive duodenocolic isthmus, and the narrow pedicle of the mesentery allows the entire midgut loop to twist around its limited attachment. This results in obstruction at the duodenojejunal junction. It occurred in eighteen of our twenty cases (Table V). The volvulus was always in the clock-

TABLE V. MALROTATION

Number of cases		20
With volvulus of midgut	18	
Without volvulus	2	
Associated peritoneal bands over duodenum	7	
Cases with gangrene	3	
Reduction and cecopexy	12	
Reduction alone	8	
Recurrence of volvulus	0	
Deaths	4	(20%)

wise direction and torsions of 180 degrees to four complete turns were seen. The tightness of the volvulus rather than the number of turns determined the severity of the symptoms.

The picture was usually that of incomplete duodenal obstruction with intermittent vomiting of copious amounts of bile-stained fluid. In over half of the cases the stools were normal. The degree of distention varied. With complete obstruction the vomiting was persistent and very little was passed by rectum.

Fig. 6.—Malrotation with volvulus. Barium enema outlines malposition of right colon. Note preponderance of small bowel shadows on right side indicated by arrows.

Plain roentgenograms often suggested the diagnosis if most of the small intestinal shadows were seen to occupy the right side of the abdomen. Malrotation of the colon was also demonstrated in some cases by barium enema (Fig. 6).

Since the superior mesenteric vessels form the pedicle around which the volvulus occurs, there may be obstruction of the vascular supply to the intestine. The symptoms and signs of strangulation obstruction ("blue-bowel syndrome") are then added to those of simple obstruction. In some instances bloody fluid may be passed by rectum. With complete occlusion of the vessels, gangrene of the entire midgut may occur. This was seen in three of our cases.

(2) Less frequently, the obstruction was due to incomplete rotation of the cecum, without volvulus of the midgut. This was found in two cases (Table V). The cecum lies in the upper abdomen and there are congenital peritoneal bands associated with this malposition. These broad bands course from the cecum or the transverse colon over the descending part of the duodenum and are attached to the undersurface of the liver or to the

posterior abdominal wall in the right upper quadrant of the abdomen. This gives rise to partial duodenal obstruction. The obstruction may be due to pressure from the overlying cecum itself.

These peritoneal bands were also found in five of the patients who had malrotation with volvulus but they were not considered to be the principal cause of obstruction in those cases.

A summary of the operative technique follows:

The entire midgut segment is allowed to eviscerate in order to visualize the pathology, and the volvulus is then reduced by turning it in the appropriate direction. This was counterclockwise in all of our cases. After the reduction is completed the congenital peritoneal bands previously mentioned are sought over the duodenum and divided if found. They are found in a significant number of cases and must always be looked for before completing the operation. In twelve of our cases the cecum was sutured to the posterolateral peritoneum in the right lower quadrant of the abdomen. In eight cases Ladd's procedure was followed in which the cecum was allowed to remain free in the left side of the abdomen after dividing the peritoneal attachments of the ascending colon.[20]

Volvulus did not recur in any of our cases nor was there any apparent difference in the course and results between the patients who had a cecopexy and the patients in whom the cecum was allowed to lie free in the left side of the abdomen. Nevertheless, from this small experience and the results seen in older children, I prefer to anchor the cecum on the right side of the abdomen if this seems anatomically feasible. The procedure has always been strongly advocated by Donovan[8] of this institution as a safeguard against recurrent volvulus since it gives a wider base of attachment to the midgut segment. There is also some advantage in knowing the position of the cecum in the event of future symptoms. One patient in this series who had the cecum fixed to the right lower quadrant developed appendicitis later. The symptoms and physical signs were classical since the organ was in normal position and the diagnosis was easily made.

Twenty patients were operated upon for intestinal obstruction due to malrotation. Four died. In three there was gangrene of the entire midgut segment, and although the volvulus was reduced further treatment was considered hopeless. The fourth death was due to postoperative pneumonia. The follow-up data on the sixteen survivals is summarized:

Two patients developed jejunal obstruction due to postoperative adhesions which required operation: five weeks later in one, and two months later in the other. The first has been followed for three years and is well. The second patient made a good recovery but has not been seen since discharge from the hospital.

One patient was operated upon for acute appendicitis three years later. He made a good recovery and is well one year following appendectomy.

One patient was asymptomatic for eight months postoperatively, 1 for one year, 3 for two years, 3 for three years, 2 for four years, 1 for six years, 1 for eight years, and 1 for nine years.

CONGENITAL NEUROGENIC ILEUS

Swenson and Bill[33] and Hiatt[17] have demonstrated that congenital megacolon is due to the lack of normal

propulsive movements of the sigmoid colon or rectum which is based on the congenital absence (or the marked diminution) of the ganglionic cells of Auerbach's plexus. This functional a mechanical cause is not demonstrated. Zuelzer and Wilson[34] have proposed to call this entity "agenesis of the myenteric plexus" and have reported on eleven illustrative cases. More recently

Fig. 7.—Marked distention in a 4-week-old baby with congenital megacolon.

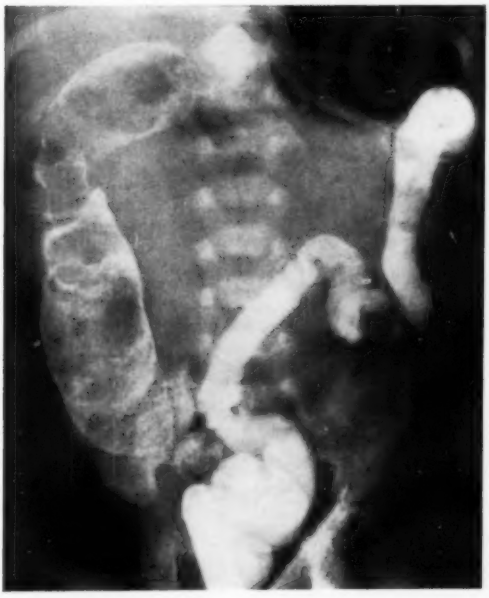

Fig. 8.—Congenital neurogenic obstruction in an 8-day-old baby. The obstruction is in the mid-transverse colon. Note dilatation proximal to this point, and the small caliber of the left colon.

type of obstruction is being recognized more readily in the newborn period in patients who present the clinical picture of intestinal obstruction in whom Potts and associates[29] presented ten cases in the newborn period with three survivals. The agenesis usually occurs in the sigmoid colon or rectum but it

can occur higher in the colon and even in the ileum. We have not found the familial incidence reported by some authors.[12, 34]

Although the symptoms varied in severity, most of the patients presented the clinical picture of low intestinal obstruction manifested by vomiting, constipation, and marked distention early in life (Fig. 7). The diagnosis was often confused with atresia or stenosis of the lower ileum or colon. The typical hypertrophy and dilatation of the bowel above the lesion which is seen in older patients with congenital megacolon was not present in the newborn period except in one case. Consequently, the barium enema was usually normal in the newborn infant, and the characteristic roentgen findings of congenital megacolon did not appear until later on. In one case the roentgenograms were highly suggestive of obstruction in the transverse colon (Fig. 8).

There were fourteen cases of intestinal obstruction due to defective intrinsic innervation in this series. The

TABLE VI. NEUROGENIC (CONGENITAL)

CASE	SITE OF OBSTRUCTION	ONSET OF SYMPTOMS	AGE AT OPERATION	OPERATION	RESULT
1.	Rectosigmoid	2 da.	2 da.	Transverse colostomy	Died.
2.	Terminal ileum	4 wk.	4 wk.	Division peritoneal band	Died.
3.	Rectosigmoid	4 wk.	4 wk.	Sigmoid colostomy	Died.
4.	Transverse colon	8 da.	8 da.	Transverse colostomy	Living 8 mo. without colostomy
5.	Rectum	3 wk.	——	None	Living 10 mo. Clinical megacolon.
6.	Rectosigmoid	6 da.	——	None	Living 9 mo. Clinical megacolon.
7.	Rectosigmoid	1 da.	1 da.	Abdomino-anal pull-through	Living 15 mo. Excellent.
8.	Cecum	1 wk.	1 wk.	Closure perforated sigmoid (enema)	
			3 wk.	Transverse colostomy	
			18 mo.	Total colectomy Ileo-anal pull-through	Living 9 mo. Frequent bouts of gastroenteritis.
9.	Rectosigmoid	3 wk.	11 mo.	Abdomino-anal pull-through	Living 10 mo. Persistent megacolon.
10.	Descending colon	4 wk.	2 mo.	Abdomino-anal pull-through	Living 2 yr. Persistent megacolon.
11.	Rectosigmoid	3 da.	2 mo.	Abdomino-anal pull-through	Living 3 yr. Excellent.
12.	Rectosigmoid	4 da.	4 da.	Transverse colostomy	
			2 mo.	Abdomino-anal pull-through	
			3 mo.	Closure colostomy	Living 2 yr. Excellent.
13.	Rectosigmoid	2 da.	3 da.	Transverse colostomy	
			6 yr.	Abdomino-anal pull-through	Living 2 yr. Excellent.
14.	Rectosigmoid	4 wk.	4 yr.	Transverse colostomy and ant. resection	
			4+ yr.	Closure colostomy	
			7 yr.	Abdomino-anal pull-through	Living 14 mo. Excellent.

diagnosis was made either at operation or at autopsy and was based on histologic evidence of agenesis of the intramural ganglia in nine cases. In the other five cases the diagnosis was made either from the highly suggestive clinical picture or from the subsequent development of typical congenital megacolon.

Many other patients with megacolon were seen during this period but only those who presented symptoms of intestinal obstruction during the first thirty days of life are included in this study.

The important features of the fourteen cases are shown in Table VI. Three patients died and eleven survived, two of whom have not been operated upon. The follow-up data are summarized in the table. The definitive operation of resection and abdomino-anal pull-through was done according to the technique advocated by Hiatt[18] of this institution.

CONGENITAL PERITONEAL BANDS

Eight of our cases of obstruction were due to congenital peritoneal bands. This group did not have malrotation. Six patients survived and two died.

The duodenum was involved in three cases. Two of these were treated by simple division of the bands while one required a posterior gastroenterostomy. These patients have been well three months, nine years, and ten years postoperatively.

Two cases of jejunal obstruction due to peritoneal bands were seen. Both patients died. One premature baby who was thought to have sepsis, and therefore was not operated upon, showed, at autopsy, gangrene and perforation of the jejunum due to a band. The other patient succumbed postoperatively after resection of gangrenous jejunum.

In three cases the terminal ileum was the site of obstruction which was relieved by division of the bands. All patients recovered, but one patient died at home four months later from intestinal obstruction due to postoperative adhesions. The other two have been free of symptoms for five and seven years, respectively.

LOCAL VOLVULUS

In a small group of cases volvulus of a loop of small intestine was the cause of obstruction. No specific etiology could be ascribed to the volvulus. In none of the cases was it associated with peritoneal bands, malrotation, or meconium ileus.

There were five patients with this form of segmental or local volvulus. Only one recovered following reduction of the volvulus and has been well for three and one-half years. The other four died after resection of gangrenous intestine and anastomosis.

MECONIUM PERITONITIS

Meconium peritonitis has been defined as a sterile reaction of the peritoneum in the newborn infant which is due to the escape of intestinal contents into the peritoneal cavity. In about half of the cases reported, perforation of the intestine has resulted from obstruction due to atresia, stenosis, malrotation, meconium ileus, or other recognizable lesion. In the other half there was no apparent obstruction and the cause of perforation was unknown, although some authors have ascribed it to birth trauma, diverticula, or some defect of the local blood supply.

The perforation often occurs during intrauterine life and closes before birth so that its location is not found at operation or autopsy. Diffuse plastic peritonitis occurs with dense adhesions and agglutination of intestinal loops. The calcification which follows is diagnostic on roentgen examination (Fig. 9). Sometimes the perforation occurs just before birth or soon thereafter. In these instances there is free meconium in the peritoneal cavity and roentgen evidence of pneumoperitoneum.

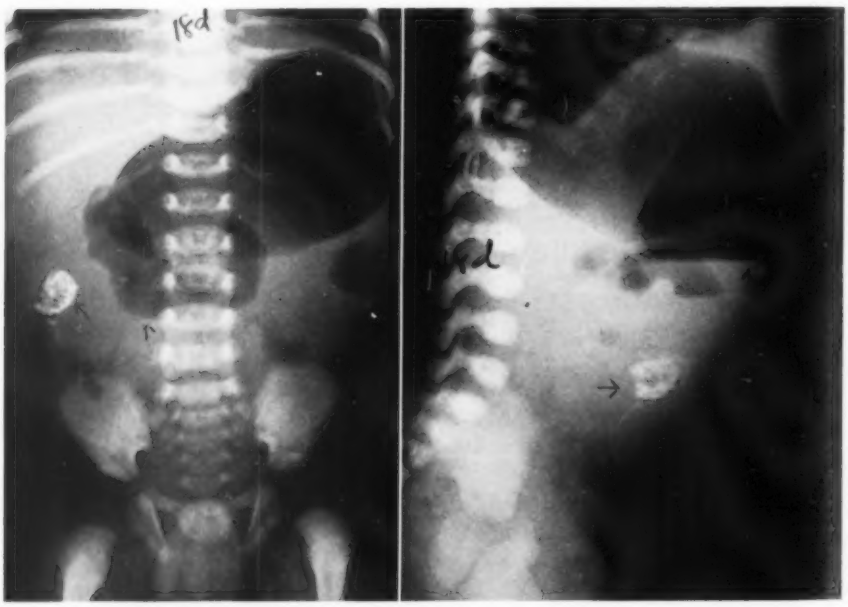

Fig. 9.—Intestinal obstruction with meconium peritonitis (calcified).

The condition has received considerable attention in recent years[4, 21, 22, 24, 27] and a few survivals have been reported.

All the cases of meconium peritonitis, in this series have been associated with obstruction. The cases in which the cause of obstruction was apparent have been previously considered in the appropriate section. In five of our cases of intestinal obstruction, meconium peritonitis was found but the specific cause of obstruction could not be determined either at operation or at autopsy. Consequently, they were considered as a separate group. It is worthy of mention that none of these patients had meconium ileus or fibrocystic disease of the pancreas.

Only one of the five patients survived. This was a 3-week-old boy who was admitted with intestinal obstruction. He had marked plastic peritonitis with dense fibrous adhesions involving all of the small intestine and there were areas of calcification scattered throughout the peritoneal cavity. Presumably, prenatal perforation of the intestine had occurred which sealed

over and he developed obstruction from the numerous adhesions that followed. The point of greatest adhesive obstruction was in the lower jejunum but the cause of the perforation could not be determined. He made an uneventful recovery following a painstaking division of all of the adhesions and release of the agglutinated loops of intestine. Except for an admission to the hospital for asthma he has been asymptomatic for five years following this procedure.

INGUINAL HERNIA

Only five patients had intestinal obstruction due to indirect inguinal hernia in the newborn period. All of them were operated upon. Three were classified as strangulated and two as incarcerated. Resection of bowel was not required in any, but orchidectomy was necessary in one case because of gangrene of the testis.

One patient made a good recovery but has not been seen since operation twelve years ago. One patient has atrophy of the testis on the side of the hernia repair eighteen months after operation. Two patients are asymptomatic nineteen and twelve months after operation. The patient who required the orchidectomy is well four months following operation.

INTERNAL HERNIA

Two patients were seen in the newborn period with intestinal obstruction due to internal hernia. In one case a paraduodenal hernia was reduced but the infant was readmitted two months later with obstruction and gangrene of the jejunum due to postoperative adhesions; he succumbed following resection. The other patient had ileal obstruction due to herniation through a defect in the mesentery of the terminal ileum. He was asymptomatic for three months following reduction of the hernia and repair of the defect but he has not been seen in the follow-up clinic for the past eight years.

INTUSSUSCEPTION

This condition is rarely seen in the first thirty days of life. Our group included three cases with obstruction. Two of the patients died. In both, the diagnosis was made at autopsy. Intussusception had followed diarrhea in the first and third weeks of life and post-mortem examination showed intussusceptions of the ileum with gangrene and peritonitis in both cases. In the one survival, operation was performed at 10 days for ileocecal intussusception. He has been well for five months postoperatively.

ANNULAR PANCREAS

There was one case of duodenal obstruction due to annular pancreas which was successfully treated by duodenojejunostomy. The patient was mongoloid and died of pneumonia six months later.

This is a rare anomaly which has been recently reviewed by Gross,[15] Conroy and Woelfel,[5] and Moore.[26]

POSTOPERATIVE ADHESIONS

Two cases of intestinal obstruction due to postoperative adhesions were seen in the newborn period. One patient developed low ileal obstruction with gangrene due to adhesions following abdominoperineal repair of an imperforate anus and recto-urethral fistula. Resection and anastomosis were required. He has been asymptomatic for fifteen months. The other patient

developed jejunal obstruction due to adhesions following repair of a congenital diaphragmatic hernia. He made a good recovery after division of the adhesions and has been well for two years.

MULTIPLE CAUSES

Three patients had intestinal obstruction from multiple causes. The first case included stenosis of the duodenum, malrotation with volvulus, and congenital peritoneal bands, all of which were considered responsible for the obstruction. At the age of 6 days the peritoneal bands were divided at another hospital but the infant continued to vomit. At Babies Hospital the malrotation with volvulus was reduced, peritoneal bands over the duodenum were divided, and a duodenojejunostomy was performed for the duodenal stenosis. She has been well for one year since operation.

The second patient had obstruction due to malrotation, congenital peritoneal bands, and volvulus of a loop of jejunum due to a large mesenteric cyst. He has been asymptomatic fourteen months following resection of the jejunum and cyst, reduction of the volvulus, and division of the peritoneal bands.

Obstruction in the third case was caused by duodenal stenosis and a congenital peritoneal band across the duodenum. The band was divided but vomiting persisted and another operation was necessary. At this time the congenital duodenal stenosis was found and a posterior gastroenterostomy was done. He made an uneventful recovery but has not been seen in follow-up clinic since discharge from the hospital four years ago.

FACTORS AFFECTING PROGNOSIS

Several factors have been responsible for the high mortality in this series:

Prematurity and associated anomalies accounted for a considerable proportion of the deaths. The incidence of prematurity (under 2,500 grams) was 10.5 per cent, and 20.9 per cent had other developmental anomalies. About half of the coexisting malformations were serious.

Shock, dehydration, electrolyte imbalance, and nutritional disturbances were prevalent factors both preoperatively and postoperatively.

Peritonitis was a common cause of death and it occurred from leakage at the suture lines or from failure to recognize and resect nonviable bowel at the time of operation.

Delay in diagnosis and operation was responsible for an indeterminate number of deaths. The delay in operation was sometimes the result of indecision on the part of the surgeon but more often it was due to the late appearance of the patient for surgical treatment.

TABLE VII. MORTALITY OF COMPARABLE SEVEN-YEAR PERIODS

YEARS	NO. OF CASES	RECOVERED	DIED	MORTALITY (%)
1939-1945	46	19	27	58.7
1946-1952	88	55	33	37.5
Total (14 years)	134	74	60	44.8

DISCUSSION

Although the mortality is still high, there has been a significant improvement in our more recent results (Table VII). Improvement can be attributed to:

(1) A better understanding of the pathology and pathologic physiology of the lesions. Recent work on meconium ileus and on the congenital neurogenic obstructions is especially noteworthy.

(2) Improved supportive treatment in the preoperative, operative, and postoperative periods. Increasing knowledge of fluid and electrolyte balance, the principle of keeping the newborn infant "on the dry side," the use of the flame photometer, and the routine use of the intravenous plastic catheter for the prolonged administration of the necessary blood and fluids have all been important factors.

(3) Improvement in pediatric anesthesia. The precarious condition of many of these infants requires the attention of a skilled anesthesiologist who has had considerable experience with this age group.

(4) The routine use of proximal decompression in the form of a nasogastric tube, a Miller-Abbott tube, or tube enterostomy.

(5) Judicious use of antibiotics. Terramycin or a combination of penicillin and streptomycin has been found the most useful.

(6) Adequate preparation for operation. Decompression of the stomach by a nasogastric tube, early "cut-down" into a vein for the insertion of a plastic catheter to correct dehydration and electrolyte loss, and the routine administration of vitamin K are essential. The preparation should not be prolonged, and these measures need not take more than a few hours in order to have the infant in the best possible condition for operation.

(7) Improved care of the premature infant. Appreciation of the altered physiology in this age group and the use of the Chapple type of incubator (Isolette) have been important. The advantages of the Isolette as demonstrated in the premature nursery at Babies Hospital under the direction of Dr. Richard Day have been: protection from air-borne and direct droplet infections, maintenance of high relative humidity and constant temperature because of the closed-circuit system of ventilation, the facility of delivering high concentrations of oxygen, and the ease of observing the infant through the lucite walls.

(8) The earlier recognition of obstruction. Although there has been some improvement in diagnosis, comparison of this factor in the early and late groups in this series has been disappointing. There is room for a great deal of improvement here.

SUMMARY

A review of 134 consecutive cases of intestinal obstruction in the newborn period seen over a fourteen-year period is presented and the various causes are discussed. Follow-up data on the survivals are recorded.

The mortality rate was 44.8 per cent. It fell from 58.7 to 37.5 in comparable seven-year periods.

The high mortality was due to delayed diagnosis, prematurity, co-existing anomalies, peritonitis, shock, dehydration, electrolyte imbalance, and nutritional disturbances.

The value of adequate supportive measure, intestinal decompression, the use of antibiotics, better care of the premature infant, and the importance of an experienced anesthesiologist are stressed.

A plea is made for the earlier recognition and treatment of intestinal obstruction in this age group. Greater

benefits are to be derived from the closer cooperation of the general practitioner, the obstetrician, the pediatrician, and the surgeon.

REFERENCES

1. Andersen, D. H.: Cystic Fibrosis of the Pancreas and Its Relation to Celiac Disease: Clinical and Pathologic Study, Am. J. Dis. Child. **56**: 344, 1938.
2. Andersen, D. H.: Therapy and Prognosis of Fibrocystic Disease of the Pancreas, Pediatrics **3**: 406, 1949.
3. Andersen, D. H.: The Present Diagnosis and Therapy of Cystic Fibrosis of the Pancreas, Proc. Roy. Soc. Med. **42**: 25, 1949.
4. Boikan, W. S.: Meconium Peritonitis From Spontaneous Perforation of the Ileum in Utero, Arch. Path. **9**: 1164, 1930.
5. Conroy, C. F., and Woelfel, G. F.: Annular Pancreas, Surgery **29**: 902, 1951.
6. Davis, D. L., and Poynter, C. W. M.: Congenital Occlusions of the Intestines, With Report of a Case of Multiple Atresia of the Jejunum, Surg., Gynec. & Obst. **34**: 35, 1922.
7. Donovan, E. J.: Time of Election for Abdominal Surgery in Childhood, New England J. Med. **236**: 937, 1947.
8. Donovan, E. J.: Personal communication.
9. Evans, C. H.: Atresia of the Gastrointestinal Tract, Surg., Gynec. & Obst., Supp. Int. Abst. Surg. **92**: 1, 1951.
10. Farber, S.: Congenital Atresia of the Alimentary Tract. Diagnosis by Microscopic Examination of the Meconium, J. A. M. A. **100**: 1753, 1933.
11. Farber, S. J.: The Relation of Pancreatic Achylia to Meconium Ileus, J. PEDIAT. **24**: 387, 1944.
12. Forshall, I., Rickham, P. P., and Mossman, D. B.: Functional Intestinal Obstruction in the Newborn, Arch. Dis. Child. **26**: 294, 1951.
13. Gardner, C. E., Jr., and Hart, D.: Anomalies of Intestinal Rotation as a Cause of Intestinal Obstruction: Report of Two Personal Observations; Review of One Hundred and Three Reported Cases, Arch. Surg. **29**: 942, 1934.
14. Glover, D. M., and Barry, F. McA.: Intestinal Obstruction in the Newborn, Ann. Surg. **130**: 480, 1949.
15. Gross, R. E., The Surgery of Infancy and Childhood, Philadelphia, 1953, W. B. Saunders Co.
16. Hiatt, R. B., and Wilson, P. E.: Celiac Syndrome: VII. Therapy of Meconium Ileus; Report of Eight Cases With Review of Literature, Surg., Gynec., & Obst. **87**: 317, 1948.
17. Hiatt, R. B.: The Pathologic Physiology of Congenital Megacolon, Ann. Surg. **133**: 313, 1951.
18. Hiatt, R. B.: The Surgical Treatment of Congenital Megacolon, Ann. Surg. **133**: 321, 1951.
19. Hurwitt, E. S., and Arnheim, E. E.: Meconium Ileus Associated With Stenosis of the Pancreatic Ducts, Am. J. Dis. Child. **64**: 443, 1942.
20. Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infancy and Childhood, Philadelphia, 1941, W. B. Saunders Co.
21. Lee, C. M., Jr., and MacMillan, B. G.: Rupture of the Bowel in the Newborn Infant, Surgery **28**: 48, 1950.
22. Low, J. R., Cooper, G., Jr., and Cosby, L., Jr.: Meconium Peritonitis, Surgery **26**: 223, 1949.
23. McIntosh, R., and Donovan, E. J.: Disturbances of Rotation of the Intestinal Tract, Am. J. Dis. Child. **57**: 116, 1939.
24. Maguire, C. H., and Moore, W. R.: Meconium Peritonitis, Surgery **28**: 568, 1950.
25. Moore, R. M.: Acute Intestinal Obstruction in Children: Physiologic-Pathological Considerations, Mississippi Doctor **23**: 554, 1946.
26. Moore, T. C.: Annular Pancrease. Review of the Literature and Report of Two Infant Cases, Surgery **33**: 138, 1953.
27. Packard, G. B., and Reynolds, Q. E.: Meconium Peritonitis, Ann. Surg. **133**: 548, 1951.
28. Patten, B. M.: Textbook, Human Embryology, Philadelphia, 1947, The Blakiston Co.
29. Potts, W. J., Boggs, J. D., and White, H.: Intestinal Obstruction in the Newborn Infant Due to Agenesis of the Myenteric Plexus (Congenital Megacolon), Pediatrics **10**: 253, 1952.
30. Pugh, D. G.: Fibrocystic Disease of the Pancreas, Am. J. M. Sc. **210**: 681, 1945.
31. Santulli, T. V.: The Treatment of Imperforate Anus and Associated Fistulas, Surg., Gynec. & Obst. **95**: 601, 1952.
32. Silverman, F. N., and Caffey, J.: Congenital Obstructions of the Alimentary tract in Infants and Children: Errors of Rotation of the Midgut, Radiology **53**: 781, 1949.
33. Swenson, O., and Bill, A. H.: Resection of Rectum and Rectosigmoid With Preservation of the Sphincter for Benign Spastic Lesions Producing Megacolon, Surgery **24**: 212, 1948.
34. Zuelzer, W. W., and Wilson, J. L.: Functional Intestinal Obstruction on a Congenital Basis in Infancy, Am. J. Dis. Child. **75**: 40, 1948.

General References (Not Cited)

1. Arnheim, E. E.: Congenital Ileal Atresia With Gangrene, Perforation and Peritonitis in a Newborn Infant, Am. J. Dis. Child. **69**: 108, 1945.
2. Benson, C. D., and Coury, J. J.: Congenital Intrinsic Obstruction of the Stomach and Duodenum in the Newborn, Arch. Surg. **62**: 856, 1951.

3. Caffey, J.: Pediatric X-ray Diagnosis, The Year Book Publishers, 1950.
4. Donovan, E. J.: Congenital Atresia of the Duodenum in the Newborn, Ann. Surg. **103**: 455, 1936.
5. Gardner, C. E.: The Surgical Significance of Anomalies of Intestinal Rotation, Ann. Surg. **131**: 879, 1950.
6. Hansmann, G. H., and Morton, S. A.: Intra-abdominal Hernia. Report of Case and Review of Literature, Arch. Surg. **39**: 973, 1939.
7. Jolleys, A., The Diagnosis of Intestinal Obstruction in the Newborn, Brit. J. Surg. **40**: 201, 1952.
8. Judd, J. R.: Atresia of the Ileum. First Successful Case Cured by Enterostomy Alone, J. PEDIAT. **30**: 679, 1947.
9. Ladd, W. E.: Congenital Obstruction of the Small Intestine, J. A. M. A. **101**: 1453, 1933.
10. Ladd, W. E.: Congenital Duodenal Obstruction, Surgery **1**: 878, 1937.
11. Ladd, W. E., Donovan, E. J., and Gross, R. E.: Panel Discussion on Intestinal Obstruction in Infancy, J. PEDIAT. **21**: 264, 1942.
12. Norris, W. J., and Brayton, D.: Acute Abdominal Condition of Infancy and Childhood, J. A. M. A. **145**: 945, 1951.
13. O'Neill, J. F., Anderson, K., Bradshaw, H. H., Lawson, R. B., and Hightower, F.: Congenital Atresia of the Small Intestine in the Newborn, Am. J. Dis. Child. **75**: 214, 1948.
14. Potts, W. J.: Congenital Atresia of the Intestine and Colon, Surg., Gynec. & Obst. **85**: 14, 1947.
15. Snyder, W. H., Voskamp, J. R., and Chaffin, L.: Congenital Atresia of the Ileum. A Report of Five Successfully Treated Cases, West. J. Surg. Obst. & Gynec. **58**: 638, 1950.
16. Webb, C. H., and Wangensteen, O. W.: Congenital Intestinal Atresia, Am. J. Dis. Child. **41**: 262, 1931.

Psychologic Aspects of Pediatrics

THE CHALLENGE OF JUVENILE DELINQUENCY

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ACCORDING to Dr. Martha M. Eliot, Chief of the Children's Bureau, Washington, D. C., more than 1,000,000 children ran afoul of the law in 1952. Of these, 275,000 went before the juvenile courts. Another 110,000 children were brought to court by parents, schools, and social agencies. Whereas the general population of children in the 10- to 17-year age group increased only 6 per cent between 1948 and 1952, official statistics indicated that juvenile delinquency rose 29 per cent.

FALLACIES IN JUVENILE DELINQUENCY STATISTICS

Figures on the incidence of delinquency are notoriously inaccurate. Criminal codes differ in the forty-eight states; consequently what is legal in one state may be illegal in another. Moreover the criminal code in the particular state varies from time to time; consequently what is illegal at one time may be legal at another.

A further consideration is the adequacy of law-enforcing agencies. A fully staffed police force will make more arrests than an understaffed force.

Police procedures also vary from time to time. At present the police in New York City have considerable leeway in regard to making arrests of juveniles. They may use their judgment about arresting a youngster who commits an occasional minor violation or releasing him with an admonition.

Community attitudes also differ. A child who transgresses at school may be turned over to his parents or he may be reported to the legal authorities. In the former instance he would not be considered delinquent, in the latter he would.

In view of considerations such as these, it is impossible to determine with any degree of accuracy the magnitude of change in the frequency of delinquency. There is, nevertheless, an impression among students of the subject that some increase has taken place during recent years. Moreover, whether or not delinquency is on the increase, it undoubtedly presents a serious social problem. It is worthy of note that delinquency is prevalent despite an improvement in the general economic level, better housing, slum clearance, increased play facilities, a wider appreciation of psychiatric knowledge.

CAUSES

Drs. Sheldon and Eleanor Glueck,[1] who have devoted their professional careers to a number of intensive studies of juvenile delinquency, found that physical health does not seem to be a significant factor. If anything, the health of the delinquent is gen-

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erally better than that of the control group. Nor are psychiatric disorders more frequent in delinquent than control children. Economic status, low intelligence (I.Q.), membership in gangs, conflicts between a foreign culture of the parents and their American-born sons play little, if any, part in the etiology of juvenile delinquency.

It is Tappan's[3] view that an important factor in the increase in juvenile delinquency is the dwindling ability of home, church, and community to influence the individual to behave in accord with the will of the group as a whole. The state and its courts have proved to be ineffectual in curbing lawless behavior.

Mr. J. Edgar Hoover,[4] Director of the Federal Bureau of Investigation, has expressed a similar view. He says: "Juvenile delinquency is a reflection of the moral tone of the nation. Young people can't be expected to behave if their elders don't. A society which produces a high incidence of divorces, broken homes, illegitimate births and adult crime creates juvenile misbehavior. Remedial action can only come from a renewal of civic responsibility. This responsibility must start in the home. There is no alternative."

An added consideration is the undue prolongation of the schooling period for the large number of adolescents who are not book learners. For such youngsters the average school is a bore. They learn nothing themselves and they interfere with the progress of the more studious ones. Nevertheless they must remain at school because of compulsory school laws.

Such boys often have a disrupting influence on the school activities. They clown in the classroom and ridicule and threaten the industrious students. Agnes E. Meyer[5] points out that "delinquency is as contagious as measles and ten times more dangerous to the health of the student body. The code that prevails in the large schools is not that of the good boys but that of the desperadoes."

An unsuccessful attempt to prevent delinquency in children through psychotherapy of the "predelinquent" has been reported by Teuber and Powers.[6] They compared the results of treatment, in a group of boys aged 6 to 10 years who were rated as likely to become delinquent, with the results in a similar group of boys who remained untreated. All the boys came from underprivileged areas in Cambridge and Somerville, Mass., and were matched for age, intelligence quotient, school grade, delinquency rating, ethnic and socioeconomic background, and other factors.

Treatment activities ranged from a friendly relationship of the big-brother variety to formal therapeutic interviews. As the study progressed treatment became more and more similar to that of the more orthodox guidance centers.

The results in the two groups were compared in 1948 after treatment had lasted 2 to 8 years in individual cases, with a median duration of 4 years 2 months. At this time the average number of court appearances for the treated group since the beginning of treatment was 2.7, for the control or untreated group 2.4. Similarly the number of repeaters appearing before the Crime Prevention Bureau was greater in the treated than the untreated group. In view of these findings, the authors conclude that "the

burden of proof is on everyone who claims specific results for a given form of therapy'' in juvenile delinquency.

A CASE HISTORY

The seriousness of the delinquency situation was dramatized recently by an outbreak of violence at a junior high school in Washington, D. C.

On Nov. 11, 1953, a 14-year-old boy nicknamed ''Sunshine'' was arrested and charged with robbing students at the junior high school of sums varying from 5 cents to a dollar.

This had been going on since the beginning of the school year. At first Sunshine had tackled the small boys but later on he extended his extortions to the bigger ones who had more pocket money. Some sixty or seventy children had given him money but they were so terrified of the bully that they told no one about their experiences.

Practically all the students knew what was going on and reports about Sunshine's extortions even reached the principal. He had called the boy into his office and warned him but, in the absence of proof, he was unable to take more drastic action.

On November 11, Mike, one of the pupils, went to the principal and asked for a dollar. He had been told by Sunshine to produce a dollar at 3 p.m. or take a beating. The police gave Mike a marked dollar which he turned over to Sunshine who was thereupon arrested.

Word got around that Mike was responsible for the arrest. Two days later he and two companions were waylaid by friends of Sunshine and severely beaten.

Sunshine's case history is a fairly typical one. He comes from a broken home. His parents were divorced when he was 3 or 4 years old, and his father is now in a psychiatric institute. Of the four children in the family Sunshine is the only one who has given trouble.

The behavioral difficulties seem to have started when he entered school. Because of a reading disability he was unable to grasp the schoolwork. He expressed his dissatisfaction by truancy and rebellious behavior. It was not until he reached high school that his reading disability was recognized and he was given remedial training but it was then too late to correct patterns of behavior which had already been established.

THE NEW YORK STATE PLAN FOR DELINQUENCY PREVENTION[7]

In 1945 a Youth Commission was established in New York State to combat delinquency. The Commission is made up of a chairman, and the heads of seven state agencies—Correction, Education, Health, Labor, Mental Hygiene, Social Welfare, and Parole Board. These agencies pool their knowledge, resources, and interests in a concerted effort to prevent juvenile delinquency. The plan has been for the Commission to undertakes studies and to act as a clearinghouse of materials which have statewide application and use, and to assume responsibility for guidance, leadership, and financial assistance to municipalities. The operation and administration of delinquency prevention programs are the responsibility of the local communities.

Much effort has been directed toward expanding recreational activi-

ties. The municipalities have spent about $12,000,000 and the state has contributed an additional $4,500,000 for this purpose. The recreational activities consist of games, sports, social activities, music, dramatics, arts and crafts, nature, aquatics, outings, camping, special events, and community service activities.

Whether this program helps to reduce juvenile delinquency may be doubtful, but it ought to make life more pleasant and meaningful for a great many children.

Another attack on juvenile delinquency has been made through youth bureaus. These are community agencies which have been created to coordinate and supplement the activities of public, private, and religious agencies devoted to the welfare of youth. Such bureaus have been set up in a number of cities and counties in New York State. They help to locate and to obtain treatment for maladjusted children. They also seek to expand public and private youth services. They keep the public informed—through the press, the radio, television, movies, meetings, and publications—concerning the needs and problems of young people. In addition they undertake studies to identify high delinquency areas, to determine the type of services most needed in such areas, and to evaluate the success of various services. And finally they encourage the coordination and integration of public and private services.

The Youth Commission has also interested itself in the laws and services affecting young offenders and has made suggestions for improving personnel policies of the reformatory type institution, for increasing professional staffs of certain institutions under the jurisdiction of the Department of Correction, for comprehensive revision of sentencing procedures, and for strengthening probation services.

In addition the Youth Commission has undertaken a study to identify symptoms in elementary school children which might be indicative of later delinquency. Spence[8] has reported the results of a study of 5,000 children attending grades 3 through 8. The factors used in this study were: extreme aggressiveness or withdrawn behavior as determined by teachers, extreme aggresiveness or withdrawn behavior as determined by classmates, truancy, unpopularity with classmates, age and I.Q. deviations from class average, reading disability, arithmetic difficulty.

TABLE I. OFFICIAL DELINQUENCY CASES IN NEW YORK STATE

	NO. OF CASES	RATE PER 1,000
1938	9,513	5.16
1939	10,199	5.56
1940	8,764	4.82
1941	9,329	5.16
1942	9,806	5.46
1943	12,772	7.16
1944	12,070	6.71
1945	12.164	6.90
1946	11,137	6.36
1947	8,740	5.02
1948	8,933	5.17
1949	8,647	5.03
1950	7,951	4.66
1951	9,366	5.31
1952	9,473	5.21

Rate per 1,000 children from 7 through 15 years of age.

Spence found that slightly more than 2 per cent of the children surveyed appeared before children's courts within three years after completion of the study. Aggressiveness was more often related to subsequent delinquency than withdrawn behav-

ior. Whereas only 5 per cent of the children were truants they made up 25 per cent of the delinquents. Particularly vulnerable were the children who were considered socially isolated by reason of unpopularity with their classmates. They made up 18 per cent of the total group but constituted 40 per cent of the delinquents.

The data on the frequency of delinquency in New York State are shown in Table I. The figures are not strictly comparable with those of Dr. Eliot's, since the age range which she discussed was 10 through 17 years, whereas the age range in the New York compilations is 7 through 15 years. The New York figures show an increase in the delinquency rate between 1944 and 1947 after which the rate fell to prewar levels and has remained there. Since 1945, when the Commission was created, the incidence of official delinquency cases has fallen from 6.90 per 1,000 children to 5.21 in 1952. This fall, however, has not been progressive. Indeed, since 1947, there has been no improvement. It is, nevertheless, heartening that, while juvenile delinquency has been rising elsewhere in the states, it has not increased in New York State.

REFERENCES

1. Eliot, M. M.; New York Times, Nov. 25, 1953.
2. Glueck, S., and Glueck, E. T.: Delinquents in the Making, Paths to Prevention, New York, 1952, Harper & Bros.
3. Tappan, P. W.: Juvenile Delinquency, New York, 1949, McGraw-Hill Book Co.
4. Hoover, J. E.: United Press Rep., Nov. 9, 1953.
5. Meyer, A. E.: The Washington (D.C.) Post, Dec. 6, 1953.
6. Teuber, H. L., and Powers, E.: Evaluating Therapy in a Delinquency Program, in Psychiatric Treatment, Proc. Assoc. Res. in Nerv. & Ment. Dis. **31**: 138, 1951.
7. Anonymous: Blueprint for Delinquency Prevention, New York State Youth Commission, Albany, N. Y., 1953.
8. Spence, R. B.: Reducing Juvenile Delinquency—What New York State Schools Can Do. New York State Youth Commission, Albany, N. Y., 1952.

Comments on Current Literature

ASEPTIC MENINGITIS

INCREASING interest in the various aspects of virus disease, particularly with the recent development of simpler and more readily available laboratory techniques, has tended to focus the attention of physicians on the role of a virus diagnostic laboratory in clinical medicine.

In the case of patients with infection of the central nervous system, presumably of virus origin, material is frequently available for virus study. A report in the *Annals of Internal Medicine*,[1] by Adair, Gauld, and Smadel, summarizes the results of such viral studies carried out over a period of eleven years on a total of 854 patients who showed clinical manifestations of "acute aseptic meningitis." The cases selected for study satisfied the clinical features listed originally by Wallgren[2] in 1925 as diagnostic criteria for aseptic meningitis. Wallgren's criteria are given as follows:

TABLE I. WALLGREN'S CRITERIA FOR ASEPTIC MENINGITIS

I. Acute onset with obvious signs and symptoms of meningeal involvement.
II. Alteration of cerebrospinal fluid typical of meningitis. The cerebrospinal fluid may show a small or large number of cells.
III. Absence of bacteria in cerebrospinal fluid, as demonstrated by appropriate direct or cultural techniques.
IV. Relatively short benign course of illness.
V. Absence of local parameningeal infection (otitis, sinusitis, trauma, etc.), or a general disease which might present meningitis as a secondary manifestation.
VI. Absence from the community of epidemic disease of which meningitis is a feature.

During the eleven-year period specimens were received on approximately 1,300 patients. However, as is so often the experience, about one-third of the cases could not be included in the analysis because of inadequate records, or because of unsuitable or insufficient specimens. Study of the 854 selected cases which were included in the analysis yielded valuable information. In general, the laboratory studies undertaken involved: (1) the demonstration of type-specific antibody in blood serum samples obtained at optimal times in the course of the clinical illness, preferably multiple serum samples taken at intervals so that differential increasing antibody titer could be demonstrated; (2) attempts to isolate the etiological agent from cerebrospinal fluid, blood, or in some instances, brain tissue obtained at autopsy.

The laboratory procedures employed in this eleven-year study varied with the years, depending upon new developments in methods and techniques. In investigating cases for evidence of infection with the virus of lymphocytic choriomeningitis, virus isolation was accomplished by appropriate animal inoculation, complement fixation and neutralization procedures being used in testing serum samples. In studies concerning mumps, a complement fixation method utilizing an antigen prepared from parotid-gland tissue of monkeys infected experimentally with the Enders' strain of mumps virus proved to be a practical procedure. In a few instances, isolation and identification of mumps virus were attempted by means of the embryonated hen's egg, and by hemagglutination and hemagglutination inhibition. In the case of herpes simplex the embryonated egg was very useful, and egg neutralization tests gave satisfactory results. In studies concerned with leptospiral infections the microscopic agglutination-lysis test was employed to advantage.

While the statistical results of this impressive study are presented in de-

tail in their publication, for purposes of summary, the authors state that in the eleven-year period, 1941 to 1952, approximately 9 per cent of these cases of "aseptic meningitis" resulted from infection with the virus of lymphocytic choriomeningitis, and 12 per cent from infection with mumps virus. Studies since 1950 on one portion of the patients included in this series indicated that about 5 per cent of the infections were due to the virus of herpes simplex and about 7 per cent to the leptospires. The notation is significant that, even with the special laboratory procedures available, approximately three-fourths of the cases of "aseptic meningitis" remained undiagnosed so far as exact etiology was concerned.

In addition to a statistical analysis of the laboratory studies pursued in connection with these cases, the authors present summaries of the clinical findings in those patients whose infections were shown to be due to lymphocytic choriomeningitis, mumps meningoencephalitis, herpetic meningitis, and leptospiral meningitis.

Tabulation of the clinical manifestations in seventy-nine cases of lymphocytic choriomeningitis revealed that the predominate symptoms and signs were headache, fever, and stiff neck. However, not all patients with proved LCM virus infection developed nuchal rigidity, in which case other clinical features suggested central nervous system involvement, prompting diagnostic lumbar puncture and laboratory studies. Approximately 35 per cent of the patients presented a definite history of prodromal illness occurring, on the average, ten days prior to the onset of meningitis. Two patients, in whom the etiological diagnosis of lymphocytic choriomeningitis was made, succumbed, one fourteen days, and the other nineteen days following the onset of their respective illnesses. In one of these, respiratory paralysis occurred associated with ascending paralysis, and in the other, bulbar paralysis occurred. In general, complications and residuals following the acute illness were few, although two patients did develop parkinsonism, one in a period of six months following recovery from acute episode, and the other in a period of about two years. Spinal fluid findings were of considerable interest, in that a significant number (nineteen of the seventy-two specimens analyzed) showed a spinal fluid sugar below 50 mg. per cent. The lowest sugar level observed was 17 mg. per cent. Isolation of virus from the spinal fluid was successful in twelve of twenty-four attempts; in one instance virus was recovered from a specimen of spinal fluid in which the verified cell count was reported as two lymphocytes.

In the eighty-six proved cases of mumps infection of the central nervous system, the principal clinical findings, as in those of lymphocytic choriomeningitis, were headache, fever, and, to a lesser degree, stiff neck. Abnormal neurological signs were observed in only about one-quarter of the cases; only 50 per cent of the cases studied had evidence of parotitis at some time during the course of the illness. Approximately 24 per cent had an associated orchitis, and about 55 per cent had either parotitis or orchitis in addition to the meningitis. It is rather striking that 45 per cent of the total number of cases studied had meningeal signs only, with no other evidence of mumps infection. Complications and residuals were few; however, one adult had weakness of the right leg, thickness of speech, blindness of the left eye, and left facial paralysis during the course of acute illness, and recovery in this case was slow. "Another had clonic and tonic convulsions, spasticity, nystagmus and dysphagia in the acute phase of the illness." A third patient of this group showed hyperactivity with psychotic delusions for about six days, and two others showed evidence of myocarditis. A mean count of 410 cells was obtained for the first four days of illness, the maximum

count observed being 1,696 cells in one case. In seven instances of the seventy-six in which tests were carried out, the spinal fluid sugar value was below 50 mg. per cent. In general, the diagnosis of mumps meningitis was based on serologic evidence of recent infection; however, in one instance the virus of mumps was isolated from a specimen of cerebrospinal fluid taken on the second day of illness. The virus was identified by appropriate measures and the strain readily established.

Six cases of herpetic (simplex) meningitis are reported in this study; all were characterized by moderately severe clinical course, with severe headache and rather prolonged febrile course. Five of the six had marked nuchal rigidity and four showed abnormal neurological signs. One had convulsions and a marked memory defect, and another developed respiratory paralysis requiring artificial respiration by mechanical respirator. Recovery in all six patients was slow, but eventually without residuals.

The clinical picture in twelve cases of leptospiral meningitis reported in this series was characterized by fever averaging about eight days' duration, headache, and stiff neck. Two presented abnormal neurological signs. Recovery was relatively uneventful with no serious residual damage noted in any of the twelve cases.

In a summary discussion the authors call attention to the similarity of clinical manifestations associated with infection due to any one of the four agents studied, particularly the triad of fever, headache, and stiff neck. They point out, however, that in about 75 per cent of the total number of patients in this series, further study is required, since exact etiological diagnosis was not accomplished. A number of possible etiological agents is listed in their discussion.

RUSSELL J. BLATTNER

REFERENCES

1. Adair, Charles V., Gauld, Ross L., and Smadel, Jos. E.: Aseptic Meningitis, A Disease of Diverse Etiology: Clinical and Etiologic Studies on 854 Cases, Ann. Int. Med. **39**: 675, 1953.
2. Wallgren, A.: Une Nouvelle maladie infectieuse du système nerveux central? Acta paediat. **4**: 158, 1925.

News and Notes

In a recent Clinical Conference from San Francisco (September, 1953, page 321), a statement as to the use of intravenous hydrocortisone has led to considerable correspondence. Dr. Shaw, who presided at the Conference, writes:

"There is apparently difficulty in securing from commercial sources infusion solution of hydrocortisone which was described for use in meningococcemia and similar infections in a recent clinical conference. At the time of the publication of this article the manufacturers felt assured that this product could be supplied commercially by the time the article appeared in publication, but apparently technical details have interfered and it is the present hope that it will shortly be available for appropriate use."

New Regulations Governing Training Requirements in Pediatrics for Graduates of Foreign Medical Schools have been adopted by the **American Board of Pediatrics.**

Citizens of the United States: Effective Jan. 1, 1954, citizens of the United States of America who are graduates of medical schools other than those in the United States and Canada will be processed for eligibility for examination for certification, if they can meet all of the following requirements:

1. They are graduates of a medical school recommended by the Council on Medical Education and Hospitals of the American Medical Association.

2. They hold a license to practice in the United States.

3. They can meet the internship and residency training requirements of the Board as detailed above with the following provisions:

a. Internship and residency training must be served in hospitals approved by the Board in the United States.

b. A maximum of the internship and one year of residency training may be allowed for such experience obtained in a small list of foreign hospitals recognized by the Board. The other year of residency training must be served in a straight in-patient medical pediatric residency appointment in an approved hospital in the United States.

Citizens of Other Countries: Properly qualified candidates who are permanent residents in and citizens of other countries and are legally qualified to practice medicine there, and who have received their training in pediatrics in the United States of America or Canada, may apply for certification by the American Board of Pediatrics.

A special certificate may be issued to foreign candidates (not citizens of the United States of America or Canada) who have received their training in pediatrics in the United States of America or Canada and who are returning to their own country at the end of their training period, upon passing successfully the regular examinations of this Board, without completion of the requirement of two full years in the practice of pediatrics. This special certificate shall be appropriately identified to distinguish it from the regular certificate of this Board.

Graduates of Canadian Medical Schools: Graduates of approved medical schools in Canada and those who have received their internship and residency training in pediatrics in hospitals approved by the Royal College of Physicians and Surgeons of Canada will be eligible for examination for certification under the same regulations as those trained in the United States.

The **Cook County Graduate School of Medicine** offers three courses in Pediatric Cardiology:

Course I: The Diagnosis and Treatment of Congenital and Rheumatic Heart Disease in Infants and Children, one week starting April 19 and Oct. 18, 1954.

Course II: Roentgenology and Electrocardiography in Heart Disease in Infants and Children, three days starting April 26 and Oct. 11, 1954.

Course III: Angiocardiography and Catheterization of the Heart and Great Vessels in the Diagnosis of Congenital and Acquired Malformations in the Hearts of Infants and Children, three days starting April 29 and Oct. 14, 1954.

Detailed information may be obtained from the Registrar, 707 South Wood St., Chicago 12, Ill.

The **"V Congreso Nacional Mexicano de Pediatria"** will be held in Guadalajara, Jalisco, Mexico, May 1 to 5, 1954, at the Instituto Tecnologico. A scientific program has been arranged and interesting social functions are planned. Inquiries should be addressed to: Ramon Sanz Munoz, M.D., Apartado Spotal 1081, Guadalajara, Jalisco, Mexico.

The **Fourth Pan American Congress of Pediatrics** will be held in São Paulo, Brazil, July 15 to 21, 1954. This year's meeting will be especially interesting in that it will be held in the city of São Paulo which is celebrating its Four Hundredth Anniversary. São Paulo is also regarded as probably the fastest growing city in the world and is a very modern metropolis with a population of over 2,000,000. The Organizing Committee for the Congress and the Academy of Pediatrics has made arrangements for tours to São Paulo this summer which will be conducted by Drake Tours in cooperation with Pan American World Airways.

The Eighth Annual Meeting of the **American Academy for Cerebral Palsy** will be held on Nov. 5, 6, and 7, 1954, in Williamsburg, Va., at the Williamsburg Inn.

The **International Children's Centre** has been founded, at the initiative of the French Government, for the scientific, psychological, and social study of problems pertaining to the health of mother and child.

An Order in Council recognizing the Centre as an institution serving public purposes was enacted on Nov. 10, 1949, following the favorable opinion of the United Nations Organization, the International Children's Emergency Fund, and the World Health Organization.

The offices of the International Children's Centre are located in Paris, at the Château de Longchamp in the Bois de Boulogne (Tel.: Longchamp 26-62).

The Centre is administered by an international Executive Board of which Professor Robert Debré is the Chairman. It is managed by Dr. Maurice Gaud, Secretary General.

Its principal activities are: teaching, preventive and immunological research work, social surveys, documentation, publications, and mass education.

I. *Teaching:*

Organization of courses which bring together from thirty to seventy students from France and other countries, most of whom benefit from a fellowship granted by the Centre, who are selected by their respective governments.

During 1950, a course in Social Pediatrics, a course on the Tuberculosis of the Child, a course on Social Psychiatry of the Child were followed by fellows originating from thirty-eight countries, who received a specialized course of training in various cities of France, Great Britain, Switzerland, and Italy, given by professors from fifteen different countries.

In 1951 were held a course in Social Pediatrics, two courses on the Rehabilitation of Physically Handicapped Children (one for medical assistants, another for qualified doctors), and one course on Vaccinations against the Common Contagious Diseases of Childhood.

In 1952 the following courses will take place: a course in Social Pediatrics, a course on the Biological Diagnosis of Communicable Diseases, and a course on the Rehabilitation of Physically Handicapped Children for medical assistants.

II. *Preventive and Immunological Research Work:*

The Centre has taken over the BCG Pilot Station of Paris which regulates the dosage of the vaccine prepared by the Pasteur Institute and performs vaccinations followed up by tests and checkings in Paris and in the provinces.

Furthermore, the Centre carries on research work on the antipertussis vaccine and directs the work of a sero-immunological laboratory.

III. *Social Surveys:*

A symposium on Children's Homes and Villages took place at Megève in July, 1951; a symposium on institutions for children deprived of normal familial environment will be held in 1954, as well as two more symposia, one of which will take place at Brazzaville in July and will deal with childhood problems in tropical countries, and the other will study the administration of antibiotic drugs to children.

A study on retarded development caused in the child by the lack of maternal care is being pursued simultaneously in London and Paris.

An experiment on the cultural entertainment of children in areas which are not in direct contact with cities is in progress in a number of rural communities of the Seine-et-Marne Department.

IV. *Documentation and Library:*

In order to place at the disposal of doctors and social workers the widest possible documentation on medical and social problems pertaining to childhood, the I.C.C. has set up a Library specialized in these problems. It is essentially a reference library, the references being collected in 690 specialized periodicals subscribed to in forty countries, while the shelves of the Library support over 2,000 fundamental textbooks.

V. *Publications:*

The *Courrier* of the International Children's Centre publishes every month surveys on topical social and medico-social problems, information on international activities on behalf of childhood, and abstracts of articles published in the 690 specialized periodicals indexed by the Centre's Library. Any subscriber may secure a free of charge microfilm or a photocopy of articles in which he is particularly interested.

The I.C.C. has further started the publication of "Collected Papers and Documents," the first volume of which is devoted to "Streptomycin Treatment of Acute Tuberculosis in Children," and the second to the publication of a "Course on Social Psychiatry of the Child" (in French only). Quarterly papers on neonatal studies will be issued as from 1952, as well as a practical handbook on vaccinations, a course on the Rehabilitation of Physically Handicapped Children, and the results of the work of the BCG Pilot Station.

VI. *Mass Education:*

In the spring of 1951, the I.C.C. initiated a mass education campaign in the guise of an Exhibition designed for fathers and mothers; the Exhibition was also visited by organized staff groups of factories, business firms, workshops, and administrations, as well as by groups of teachers and their pupils.

The Exhibition displayed in a simple and striking fashion the dangers threatening infants under one year of age: the causes of infant mortality, the contagious and hereditary diseases, the errors in nutrition, and acquainted the public with the various agencies which take care of the welfare of mother and child.

The Exhibition will be shown in various cities of France and the neighboring countries.

The development of these activities is expected to enable the I.C.C. to become a documentation, study and research center unique of its kind; placed at the service of specialists the world over, the Centre will endeavor to contribute to the improvement of the physical and moral welfare of the child, only too often an innocent and helpless sufferer.

Charles H. Rammelkamp, M.D., professor of medicine at Western Reserve University in Cleveland, delivered the twenty-second annual series of the Benjamin Knox Rachford Lectureships on February 25 and 26, 1954, at the Children's Hospital Clinic and Research Building, Cincinnati, Ohio. The titles of his lectures were (1) "Acute Streptococcal Infections and Rheumatic Fever," and (2) "Acute Hemorrhagic Glomerulonephritis."

Book Reviews

Pediatric Gynecology, ed. 3. Goodrich C. Schauffler, M.D. Chicago, 1953, Year Book Publishers, 318 pages. Price $7.50.

Dr. Schauffler has been interested in this subject since 1925, and it is largely through his teaching and publication that the profession has become aware of the importance of gynecologic problems in children.

He has given a very practical outline for history-taking and examination, emphasizing the need for care in avoiding mental and physical trauma which may cause permanent damage. The importance of establishing an accurate diagnosis and instituting specific treatment, where possible, in the future well-being of the child is elucidated. The psychosomatic aspects of puberty with its problems of masturbation, adjustments to menses, social adjustments, and so forth, are brought up to date as is the treatment of vaginitis, congenital abnormalities, menstrual irregularities, and urologic problems in childhood.

In this edition there is a new chapter on embryology by Dr. C. Gordan Robertson, and the chapter on pediatric urology by Dr. Clarence B. Hodges and on general surgical consideration in children by Dr. C. W. Brunkow have been brought up to date.

This book is a valuable aid to any physician, whether he be student, general practitioner, internist, surgeon, or gynecologist. R. J. C.

Psychology in the Nursery School. Nelly Wolffheim, New York, 1953, Philosophical Library, Inc., 144 pages. Price $3.75.

The title of this book, which is translated from the German, is a misnomer. What it really consists of is an attempt to show that a nursery school should be run on Freud's psychoanalytical conceptions. While a good nursery school teacher, like the pediatrician, must have some knowledge of child psychology, we shudder to think of a young child in a nursery school where the principal is concerned with interpreting the child's behavior in terms such as "ego ideal," "instinctual renunceation," "castration complex," and our good old friend "Oedipus Complex" which are discussed in this book. Fortunately, for a number of reasons, it will have little influence on our nursery schools. B. S. V.

Eritrosedimentación. Alberto Chattás, Buenos Aires, 1953, Librería "El Ateneo," 135 pages.

A monograph in Portugese, discussing the theory and techniques of erythrosedimentation, and its application in the clinic. The final chapter discusses its place in pediatrics. There is an extensive world-wide bibliography.

Morbo di Cooley e Alterazioni Metaboliche. G. Romeo, R. Gavini, and V. Mattina, Catania, Italy, 1953, Revista Pediatrica Siciliana, 110 pages.

A monograph in Italian, with summaries in English and German, of metabolic studies on eight cases of thalassanemia major. Studies were made of gastric and pancreatic function, and on the absorption of carbohydrates, fats, proteins, Ca, and P, because of the association of celiac disease with erythroblastosis (Bennett's disease) and cases of Cooley's disease in which celiac disease developed. Briefly the findings were hypochlorhydria in 75 per cent, normal trypsin, steatorrhea with low fat absorption, and a flat amino acid curve using West's test with gelatin. They also found some deficiency in carbohydrate absorption. Blood Ca was normal with a moderate hypophosphatemia. They consider that the low fat absorption may involve a low vitamin D absorption and that this may play a part in the alterations of the bone in thalassanemia. Thus they suggest that the same metabolic disturbance is involved in the production of symptoms common to the two diseases.

A Study of the Visual Perception of Deaf Children. H. R. Myklebust, Ed.D., and Milton Brutten, Ph.D., Lund, Sweden, 1953, Supplement 105, Acta Oto-Laryngologica.

A monograph of a study by Drs. Myklebust and Brutten of Northwestern University of the visual perception of deaf children. The authors found that deafness impairs visual perception which may lead to learning problems in the deaf child.

Editor's Column

IS "NONPARALYTIC" POLIO UNCOMMON?

AN INTERESTING viewpoint in regard to nonparalytic cases of poliomyelitis which runs counter to the generally accepted viewpoint is presented by Shaw and Levin in this issue. The authors, in a study of 798 cases observed at the Children's Hospital in San Francisco, reached the conclusion that in nearly every instance where a diagnosis of polio can be made from the clinical findings, a careful, thorough examination will show muscle weakness. In other words, nonparalytic polio is extremely rare. The question of the thousands of individuals who, from immunization studies, seemingly have been exposed to a polio virus without developing clinical symptoms of the disease is not at issue or involved, nor are the nonspecific illnesses seen during epidemics without definite signs of central nervous system involvement which are regarded by many as cases of nonclinical polio infections. It involves only those cases in which the diagnosis from the clinical findings in all probability is polio.

Stokes in his discussion of polio in Mitchell-Nelson (1950) uses the term "abortive" poliomyelitis for nonparalytic cases. "In the majority of instances . . . the disease subsides in the second stage without the production of paralysis." He further states, "No method at present for establishing the diagnosis of poliomyelitis exists in such cases aside from the isolation of the virus from the nose or throat or from the stools, an impractical procedure under ordinary conditions." Ward, in the discussion of polio in Holt-McIntosh (1953), considers that for every paralytic case of polio there are 10 to 100 infected individuals who are not paralyzed. These he divides into three groups: healthy carriers, abortive, and nonparalytic. He terms as abortive the nonspecific illnesses with no signs of central nervous involvement. The term nonparalytic is used for those cases which have symptoms of an infection similar to the abortive, but, in addition, stiffness and pain in the neck and extremities, and increased cells and protein in the spinal fluid. He likewise emphasizes that there is no simple laboratory test by which the clinical diagnosis can be confirmed. It is Shaw and Levin's viewpoint and contention that in the cases where a diagnosis of polio can be made from the course, clinical findings, and spinal fluid, a careful examination will disclose some muscle weakness (paralysis), and, hence, nonparalytic poliomyelitis is uncommon. They present in some detail the rather simple methods of testing for muscle weakness used in their hospital which led to the findings presented in the study. A recent report published after their study was completed, by Moskowitz and Kaplan of the Grasslands Hospital in New York, tends to support their findings and viewpoint. This study was based on "follow-up" findings rather than on the examination during the acute stage in the hospital.

The point raised is an important one. If these findings and views become accepted, the so-called "nonparalytic"

cases require more therapeutic work than they usually receive. It further calls for a more complete examination for muscle weakness for all cases, and particularly for those in which paralysis is not obvious.

* * * * * *

In order to obtain the viewpoint of others, the report in proof, together with the editorial to this point, was submitted to a number with a large clinical experience in polio, and their comments invited.

Dr. Robert L. Bennett of Warm Springs Foundation comments as follows:

I am in hearty agreement with Drs. Shaw and Levin. I believe that the percentage of nonparalytic cases of acute anterior poliomyelitis listed in any statistical record will depend on relationship between the criteria for the diagnosis of acute anterior poliomyelitis and the ability to determine weakness during the acute stage, plus the ability and facilities to follow through by routine examination every few months those cases listed as "nonparalytic." I believe the important point to be emphasized is that very few of us are able to pick up mild changes in strength or pattern of action during the acute stage or even during the early convalescent stage. Many patients who developed serious weakness and perhaps even more serious deformity later were those who were diagnosed as having no paralysis during the acute stage and those who were not followed because of this erroneous nonparalytic assumption. Many patients with mild weakness are permitted increasing activity during the time when strict rest should be enforced. These patients may develop increased weakness as a direct response to overuse of weakened muscles that would have had an excellent chance of complete recovery if properly protected during the early convalescent phase. As a result of failure to recognize mild weakness and to enforce restriction of activity, many patients may have residual weakness and deformity for the rest of their lives. I do not believe that all so-called "idiopathic scoliosis" are sequelae to acute anterior poliomyelitis, but I have seen many scolioses develop with particular patterns characteristic of those following acute anterior poliomyelitis in individuals who were said to have had nonparalytic poliomyelitis.

Dr. Harold K. Faber of San Francisco comments as follows:

The observations of Shaw and Levin are in harmony with a view that I have held for many years, that when poliomyelitis infection reaches the stage of clinical manifestations, no matter how mild, it has already invaded the central nervous system. Experimental work, indeed, indicates that such invasion can occur even without detectable clinical signs. In mild "nonparalytic" poliomyelitis, changes in the cerebrospinal fluid are very common and provide positive proof that the central nervous system is infected, while absence of such changes does not exclude the possibility. The studies of Bodian have shown that whenever central nervous system infection has occurred, a very large proportion of the motoneurons in the spinal cord enlargements show microscopically visible signs of infection regardless of the severity or mildness of the accompanying paralysis. The saving grace of poliomyelitic infection is the reversibility of the pathological process in a large proportion of the affected motor cells, which in milder grades of involvement are able to carry on their functions with only slight impairment and in severer grades are often able to recover with parallel recovery from paralysis. The fact that all gradations between slight transient weakness and permanent flaccid paralysis occur in the human disease points to the identity of the underlying pathological process in mild and severe cases, and it is not really surprising to find that when patients are examined, as Drs. Shaw and Levin have done, carefully and

consecutively during convalescence, some areas of weakness or paralysis are found in nearly all of them.

It is only in the asymptomatic cases, detectable only in retrospect by tests for neutralizing or other specific antibodies, that one may be fairly sure that invasion of the central nervous system has not occurred. In the cases with clinical manifestations the use of such descriptive terms as "mild," "minor," "abortive," as indicative of a "systemic" or "extraneural" site of the infection is obviously misleading.

Dr. Horace L. Hodes of New York comments as follows:

There can be no disagreement with the authors' views regarding the importance of careful examination of the muscle function of all patients with poliomyelitis. Furthermore, such examinations should be made during the acute and convalescent stage and at regular intervals after the active phase of the disease has subsided. It is certainly true that a number of patients considered to be nonparalytic during the early convalescent stage of polio will be shown by subsequent examination to have suffered some loss of muscle function. Good medical practice requires that every effort be made to prevent such errors in order to provide treatment which may be expected to yield the greatest chance of recovery.

The data concerned with the relative frequency of nonparalytic as compared with paralytic poliomyelitis are very interesting. In a general way, they are in accord with over-all statistics which suggest that a larger percentage of patients do in fact become paralyzed at the present time than was formerly the case. Whether this is related to the shift of age incidence, to better examination, or to mutation of the virus, cannot be stated.

Shaw and Levin follow the same definition of nonparalytic poliomyelitis which most authors use; it appears to be the same as that quoted from Ward in the editorial above. The term is reserved for patients showing evidence of central nervous system disease without paralysis or muscle weakness. The term "nonparalytic" means that there may be injury to neurons, but that the injury does not involve a number of neurons large enough to produce clinically detectable muscle weakness. The term excludes the healthy carrier and the patient without symptoms of central nervous system (such as stiffness of the neck and abnormal spinal fluid).

Some reservations must be expressed regarding the conclusion of the authors that the statistics presented indicate that only "a small proportion of those patients in whom the original diagnosis can be established will completely escape muscle weakness." For example, the figure of 3.9 per cent of nonparalytic patients cannot be taken at face value, since it is obtained from a consideration of 798 patients of whom 517 were already paralytic on admission. That artificial selection has operated here may be assumed. The authors state that 11 per cent of the 281 patients who were preparalytic remained nonparalytic. It is impossible to evaluate this figure with any degree of assurance. A number of factors may operate to make this figure inaccurate. For example, the physicians in and around San Francisco may elect to keep at home those preparalytic patients who show only minimal systemic symptoms, while those who seem more sick might be hospitalized. Another possible source of error may very well have been errors in diagnosis which operated to make the nonparalytic group of patients appear smaller than it in fact was. In this regard, the authors excluded six patients with "Guillain-Barré syndrome," and ten patients with encephalitis of unknown etiology. Unless virologic and serologic studies were made, one cannot be certain that some of these patients were not in fact suffering from nonparalytic poliomyelitis.

Our own experience is that about 30 per cent of patients entering the hospital with preparalytic poliomyelitis do not develop detectable weakness. It is possible that the difference

between our experience and that of Shaw and Levin may be due to a difference in selection of patients for admission to the hospital or perhaps to a difference in virus strains. Since our muscle examinations are made in a manner very similar to that described by Shaw and Levin, it is probable that the method used for detecting weakness does not account for the difference between their experience and ours.

Dr. Philip M. Stimson of New York comments as follows:

My experience has been in complete agreement with practically every statement in the article of Drs. Shaw and Levin with the possible exception of their last sentence under "Comment" in which they state: "In the vast majority, however, weakness, once apparent, has been objectively demonstrable for at least two or three months." If a patient shows enough clinical manifestations of acute poliomyelitis to make a diagnosis fairly certain, I agree that a careful search done ten to twelve days after the onset of the illness will in the great majority of cases reveal at least a difference in strength between some of the corresponding muscles on the two sides of the person, more than can be accounted for by left-handedness. It has been my experience, however, that a considerable number of these minor weaknesses will disappear within the next week or two if the patient is kept from fatiguing in any way these affected muscles. In other words, the supposedly nonparalytic case of acute poliomyelitis should be kept in bed at least two weeks, and often a third week if to allow the patient gradually to be "up" would release too much activity.

Comment also might be made that elevation of the spinal fluid cell count is "revealing" only of something wrong in the central nervous system —not necessarily poliomyelitis.

As to the editorial content, objection can well be raised to the term "abortive poliomyelitis"—a diagnosis made by guesswork or presumption and comprising cases that are inadmissible to any statistical records. Either the illness under question is acute poliomyelitis with or without weakness, or it is an indefinite "characteristic minor illness" suspected only by concomitant circumstances of being a poliomyelitis virus infection, but not to be proved as such except by extensive laboratory methods, and also not to be listed. The sooner the term abortive poliomyelitis is dropped, the better it will be at least for statistics, and correct statistics are, of course, valuable for studying the proper treatment of the disease.

Drs. Shaw and Levin in this article have made a very valuable contribution to the care of poliomyelitis patients in again emphasizing the frequency of the presence of clinically recognizable muscle weakness when properly looked for in the great majority of supposedly nonparalytic, but quite definite clinical, cases of acute poliomyelitis.

Dr. Franklin H. Top of Iowa City and formerly of Detroit comments as follows:

Drs. Shaw and Levin's findings are difficult to accept as they run counter to ordinary experience. Their Tables I and II show few admission preparalytic cases dismissed as nonparalytic cases. I include a table which shows the dismissal status of cases in three periods, 1940-1944, 1945-1949, and 1950-1952. During the 1940-1944 period a follow-up clinic was not in operation to check on dismissal nonparalytic cases. In 1945-1949 the following procedure obtained, namely, muscle check on each case admitted by house staff and director, and within twenty-four hours by the head physiotherapist; thereafter, when possible, three examinations per week until dismissal when a dismissal check was made. After discharge, each patient returned at one month, three months, six months, and again at a year. During the period 1950-1952 I was not at the Herman Kiefer Hospital, but careful checks are still made in the hos-

pital, although the extensive follow-up system has been modified.

It is interesting in the light of the varied procedures above to compare the proportion of nonparalytic cases during each period. To be sure, this is not broken down by pre-admission diagnosis as Drs. Shaw and Levin have done, but the conclusion to be drawn is clear, namely, that in three consecutive periods the final proportion of nonparalytic cases varied between 33.7 and 45.8 per cent. In addition, in the period 1945-1949, during which the most stringent muscle check and follow-up procedures were carried out, the proportion of nonparalytic cases was greatest for the three periods in question. As an aside, I must call attention to the fact that during all three periods more than 85 per cent of all reported cases in Detroit, Wayne County, and Macomb County (population roughly 2,000,000) were hospitalized at the Herman Kiefer Hospital. I do not have similar data for subsequent years but I can assure you that careful analysis of admitted patients has continued since the period in question. Our data do not duplicate the experience of Moskowitz and Kaplan who found more than one-third of patients on follow-up to have weakness undetected before dismissal. Our proportion of such findings would be more nearly 5 per cent, though this is not an exact figure.

In the light of the above data from the Herman Kiefer Hospital, I believe that the following factors may be operative to explain the experiences Shaw and Levin cite:

1. *Many mild cases are not sent to hospital.* What proportion of the total reported cases of poliomyelitis in San Francisco and environs are seen at the Children's Hospital? The answer to this question is important in order to get a complete picture. However, the local and nonlocal admission preparalytic cases in Shaw's Tables I and II indicate a fair proportion of admitted cases in that category but *few* designated as nonparalytic. This proposition, therefore, does not appear likely.

2. *Interpretation of muscle power too rigid.* The tests carried out (page 241) during the second or third week on a patient continuously bedridden would likely show weakness in patients other than those with poliomyelitis. I believe, as Shaw and Levin do, that any weakness changes a nonparalytic patient to the status of paralytic. However, I wonder if the criteria of weakness used by him are perhaps too stringent. I do not believe that physiotherapists can determine muscle power within 80 to 100 per cent of normal even if they were apprised of the preillness status of each patient they see. Time would not permit of determining the power in each muscle, and other factors such as right- or left-handedness must be considered as well as the length of stay in bed. Perhaps this paragraph does not apply for I am ignorant of the criteria used by Dr. Shaw and his staff.

POLIOMYELITIS. HERMAN KIEFER HOSPITAL, DETROIT, 1940-1952
FINAL CLINICAL STATUS OF CASES IN THREE PERIODS

PERIOD	SPINAL	BULBAR	BULBO-SPINAL	ENCEPH-ALITIC	NON-PARALYTIC	TOTAL	% NON-PARALYTIC
1940-1944	228	85	64	3	193	573	33.7
1945-1949	446	161	124	14	629	1,374	45.8
1950-1952	907	130	189	9	834	2,069	40.3
Total	1,581	376	377	26	1,656	4,016	41.2

3. *Patients with spasm but without weakness are counted as paralytic cases.* This does not appear likely from reading the article.

4. *Persistent spasm of one muscle may cause weakness in an opponent or associated muscle.* Where spasm occurs and remains for a period of several weeks or longer, any associated muscles not affected by spasm or weakness may be limited in motion and undergo beginning atrophy from disuse which in turn may appear as weak-

ness. Such cases are not counted by us and do not form a large proportion of the nonparalytic experience.

5. *A different type of poliomyelitis is present in San Francisco and its environs.* This can happen as witness the outbreak of alleged poliomyelitis in the Los Angeles area nearly two decades ago.

Summary.—From the epidemiological and clinical points of view, I have no sound reasons for believing that the spectrum of infection in poliomyelitis is so narrow in the mild and moderate illness range as to finally exclude nearly all cases which are admitted to hospital as preparalytic poliomyelitis. There is ample evidence to indicate that most infections are at an inapparent or subclinical level and further that many illnesses go unrecognized as poliomyelitis. The next category in the infection spectrum is the mild and recognized case, followed in order of severity by lower center paralysis, by higher center paralysis, by a mixture of the last two and by death. There is, indeed, a diminishing number of affected individuals as the more serious end of the spectrum is approached, but a sharp narrowing of bonafide instances of infection in the nonparalytic range does not appear likely and is not borne out by the bulk of clinical experience based on careful evaluation of muscle power by both clinicians and physiotherapists. The experience of Drs. Shaw and Levin, which may be valid for the experience they cite, cannot, in my estimation, be projected as common experience in all groups of preparalytic cases of poliomyelitis if more refined muscle testing or greater clinical scrutiny were applied.

I heartily agree with Drs. Shaw and Levin, however, that careful or *more* careful assessment than at present generally obtains should be carried out everywhere and that any real or questionable weakness must be considered carefully in order that adequate treatment measures may be initiated.

Dr. James L. Wilson of Ann Arbor comments as follows:

The paper by Drs. Shaw and Levin indicates that in their cases admitted in the preparalytic stage, the incidence of detectable paralysis is higher than has been generally reported. They find that over 90 per cent of all patients get some degree of paralysis. We might compare this with the results obtained years ago in Massachusetts when a large experiment with the therapeutic value of serum was carried out and all doctors were alerted to the preparalytic diagnosis of polio. Under these circumstances something like 70 per cent of all patients, detected with preparalytic poliomyelitis, developed some form of detectable paralysis under the observations of skilled muscle examiners. Drs. Shaw and Levin's figures are high therefore, although not remarkably higher than these earlier studies indicate.

The reasons for this higher than usual incidence of paralysis must be among the following:

1. That Dr. Shaw or his workers have made more meticulous muscle examinations.

2. That fewer patients with nonparalytic poliomyelitis are diagnosed and sent to their hospital than in other areas.

3. That there is an actual greater incidence of paralytic poliomyelitis in San Francisco in the years that they report than has been obtained at other times or in other places.

We, of course, can only speculate as to the difference in their findings.

In regard to the first, it is certainly true that a muscle examination, done at different times, detects different degrees of paralysis. The distinction between a pseudoparalysis in a patient who has muscle spasm, tenderness, or tightness, whichever word one pleases to use, and true paralysis is a very difficult one to make since the cooperation of the patient is absolutely necessary to a good muscle examination. It is

conceivable, not only that Drs. Shaw and Levin have detected more paralysis than most people have, but that also they have called paralysis something which other people have concluded is only a pseudoparalysis, not a true one. We can dispute, with no possibility of conclusion, as to whether a patient who cannot use a certain muscle group well at one stage when there is tenderness, and can do so later, actually had true paralysis from which he recovered, or had an inhibition of free muscle action which we have wrongly called paralysis.

In regard to the second point, it is clear from Drs. Shaw and Levin's own figures that there is a difference of almost 50 per cent in the amount of those free from paralysis who were sent to them from local areas and those from a distance. It is true, though, that in both groups there was a very high percentage of detectable paralysis, but certainly accuracy of nonparalytic diagnoses seemed to be somewhat greater in their local area. It is conceivable that there was an incidence of disease with less severe systemic reaction during the years under study in San Francisco than in other areas, and therefore fewer patients with severe meningeal signs, who did not have actual muscle paralysis, were detected than in other years.

The third supposition, that there was a greater incidence in San Francisco than in other areas, can hardly be discussed. It can only be concluded to be true if the other two premises are discounted.

All in all, Drs. Shaw and Levin are making a good point, that the more careful the examination is made, the more minor degrees of weakness of a transitory type can be discovered. We must be careful under these circumstances, of course, that we do not give credit to physiotherapy for cures from paralysis which would have taken place spontaneously.

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